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THE PROGNOSIS AND MANAGEMENT OF SUBARACHNOID HÆMORRHAGE*

JOHN N. WALTON, M.D.(Durh.), M.R.C.P.(Lond.),†
Newcastle upon Tyne, Eng.

AN INCREASING AMOUNT of attention has been paid, in recent years, to the problem of management posed by cases of subarachnoid hæmorrhage. A flurry of recent publications has advised methods varying from the ultra-radical approach (on the part of some neurosurgeons) to an extreme conservatism (advocated by some neurologists). From the welter of conflicting opinions, some based upon an uncritical acceptance of ill-digested information, it is difficult for the physician who is confronted with a patient suffering from this disorder to know which path to follow in the interests of his patient. I cannot hope this evening to present to you any final decision upon this highly controversial subject, but I would like to indicate several facts derived from a study of the prognosis of the illness in a series of patients treated conservatively, facts which seem to me to give us some guidance in our approach to the problem.

The opinions which I shall express are based upon the results which I collected when reviewing a series of 312 consecutive cases of spontaneous subarachnoid hæmorrhage admitted to the Royal Victoria Infirmary, Newcastle upon Tyne, over the 10-year period 1940-1949 inclusive.[1] Of these 312 cases only 30 were observed personally; information concerning the remainder was gleaned from case records. However, in 1951 and 1952 I was able to trace 170 of the 172 patients who survived the original illness and I interviewed and examined all the 120 patients who were still alive.[2] On 82 of the 140 patients who died of the original illness, an autopsy was performed and I was able to examine the pathological material. In addition, a scrutiny of the records of the Pathology Department from 1920 to 1939 yielded another 91 examples of this condition, so that I was able to analyze the pathological findings in a total of 173 fatal cases.

Before relating to you some of the results of my investigation and the conclusions which I have drawn from them, it might be of interest to look for a moment at one or two historical facts. Subarachnoid hæmorrhage is probably a disease of great antiquity. Indeed, there is a reference in the second book of Kings, Chapter 4, to a boy "who said unto his father 'my head, my head'—and when he had taken him and brought him to his mother he sat on her knees till noon and then died." I think that this story is very suggestive of subarachnoid hæmorrhage and there are many references to similar incidents in classical literature and in ancient medical writings. Morgagni's description[3] of the servant who collapsed when running after his master's chariot, and in whom autopsy revealed a tear in the intracranial carotid artery, is a classic example. In general, however, this condition was grouped with the other forms of apoplexy until late in the 19th century. At about this time numerous French authors, including Froin[4] and Hayem,[5] began to report instances of meningeal hæmorrhage, while many reports appeared of cases of intracranial aneurysm, some with subarachnoid and intracerebral hæmorrhage. Although Gull[6] in 1859, Bartholow[7] in 1872 and Bramwell[8] in 1886 had commented upon the frequency of the association between aneurysm and meningeal hæmorrhage it was not until the early 1920's, owing largely to the writings of Fearnsides,[9] Collier[10] and Symonds,[11] that it became generally recognized that the syndrome of spontaneous subarachnoid hæmorrhage was usually due to rupture of an intracranial aneurysm.

DIAGNOSIS AND ETIOLOGY

Here I think it is essential to pause for a moment to define my terms. It is well known that blood can appear in the subarachnoid space as a result of numerous factors, among which trauma and parenchymatous cerebral hæmorrhage of atherosclerotic origin, in addition to intracranial aneurysm, are outstanding. However, in my concept of the clinical syndrome of spontaneous subarachnoid hæmorrhage I exclude traumatic and neonatal cases in addition to those in which atherosclerotic intracerebral hæmorrhage is the primary disorder, with subsequent rupture into the ventricles and subarachnoid

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†Research Assistant, Department of Medicine, Royal Victoria Infirmary, Newcastle upon Tyne; late Nuffield Foundation Travelling Fellow in Neurology, Massachusetts General Hospital and Harvard Medical School, Boston, Mass., present address—Neurological Research Unit, National Hospital, Queen Square, London.

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space. In the latter type of case the patients are usually elderly, while deep coma and dense neurological signs such as hemiplegia are usually present from the outset. In spontaneous subarachnoid hæmorrhage on the other hand, the patients are usually younger, with a peak incidence in the 40 to 60 age group,[1] severe blinding headache and neck stiffness are most often the presenting symptoms, and neurological signs resulting from bleeding into brain substance tend to appear some hours after the ictus, not immediately. I must say frankly, however, that while this differential diagnosis is straightforward in the average case, it may occasionally be very difficult to decide whether a case is one of spontaneous subarachnoid hæmorrhage with or without intracerebral extension, or one of primary intracerebral hæmorrhage of atherosclerotic origin. Despite the occasional difficulty in making this distinction I have attempted it in selecting my series of cases in order to achieve as clearly as possible definition of the clinical features of the syndrome of spontaneous subarachnoid hæmorrhage.

I must make it clear that I did not confine myself to consideration of cases of aneurysmal rupture. This syndrome may result from a variety of pathological lesions and another of my aims was to obtain accurate information concerning the incidence of the various pathological entities responsible for the production of the clinical picture. A patient may present with the characteristic picture of spontaneous subarachnoid bleeding but it is then the duty of the physician to apply his clinical acumen and whatever diagnostic tests he may consider necessary and profitable in order to determine the cause. I reported last year[12] a series of cases of unusual etiology—subarachnoid hæmorrhage resulting from glioblastoma multiforme, from meningioma, from intracerebral metastases, from acute ulcerative endocarditis, from blood diseases and from intracranial sinus thrombosis, as well as some instances of primary spinal subarachnoid hæmorrhage resulting from vascular anomalies and tumours of the cord. In some of these patients the primary disease was evident before the bleeding episode, in others the subarachnoid hæmorrhage was the initial manifestation. In most of them the clinical picture was indistinguishable from that due to rupture of an aneurysm.

Within recent years, angiographic studies have revealed the importance of previously asymptomatic intracranial angiomas as a cause of this syndrome. In some series,[13, 14] as many as 20 to 30% of cases have shown such lesions. The incidence of angioma is much less in autopsy material (3% of my fatal cases) but this may be related to the fact that angiomas tend, in general, to bleed little and often and the prognosis in most such cases is less grave than that of aneurysmal rupture. My conclusion from my own series and from a review of the literature is that the syndrome of spontaneous subarachnoid hæmorrhage is a result of aneurysmal rupture in about 80% of cases; it is caused by rupture of an intracranial angioma in perhaps 10% and by a variety of pathological conditions in the remaining 10%. I think it is worth pointing out here that the aneurysms which are large and give rise to signs of a space-occupying lesion, the so-called "paralytic" group of Meadows,[15] do not often rupture to give this clinical picture. Large aneurysms within the cavernous sinus do bleed, but when this occurs, hæmorrhage is confined by the walls of the sinus, giving the typical picture of pulsating exophthalmos, but there is no extension as a rule to the subarachnoid space. Most aneurysms giving rise to subarachnoid hæmorrhage are previously asymptomatic and the same applies to a considerable proportion of angiomas. I make these points since the information I have given you about etiology will clearly have a bearing upon management.

I do not propose to dwell upon the clinical and pathological features of this illness as I am sure most of them will be familiar to you all. However, one or two points are worthy of brief mention in view of the influence they have upon the course of treatment to be adopted. In particular it is important to consider what clinical features may be of help in deciding upon the nature and situation of the causal lesion. Firstly, when confronted with a patient suffering from this clinical syndrome the possibility that the condition may be due to one of the unusual causes already mentioned should be borne in mind. Like so many other conditions, this is one in which we should remember that as physicians and surgeons we are concerned with the whole patient, and not just with that portion which lies within the skull and spinal canal. In such a case careful history-taking and a complete

physical examination may reveal signs of anæmia or of bleeding into skin or mucous membranes to suggest a blood disease. On another occasion a history of vague headaches, of personality change or clumsiness of a limb may bring to mind the possibility of an intracerebral neoplasm as a cause of the bleeding. Or fever and cardiac murmurs may raise the possibility of bacterial endocarditis. Many other variations occur from time to time, but I do not wish to be too particulate; it is sufficient to say that one should be on the alert for such signs of general medical disease which may be the cause of the hæmorrhage and may require definitive treatment. In the absence of features of this type it is justifiable to assume that the bleeding is due to a ruptured aneurysm or angioma. Can one then differentiate on clinical grounds between these two? It is often quite impossible to make this distinction; several authors have pointed out that many bleeding angiomas are very small and otherwise asymptomatic. Of course it is true to say that a history of multiple previous bleeding episodes, of focal seizures and progressive neurological deficit (e.g. hemiplegia) favours angioma, while a cranial bruit, if heard, is virtually diagnostic. Similarly, a long history of typical attacks of migrainous headache, invariably occurring on one side of the head, is professed by some patients with intracranial angiomas, but occasionally the same is true of patients with intracranial aneurysms, particularly those on the internal carotid artery. Furthermore, many angiomas, being situated within cerebral substance, tend to produce more direct brain damage and hence neurological signs when they bleed than do aneurysms; although this comparison is statistically valid in a large series of cases it is of little value in the assessment of an individual case. I think we can conclude that whereas occasionally there are clinical features to suggest an angioma rather than an aneurysm as the cause of bleeding, in the great majority it is impossible to be sure which is present. Of course, as my figures have shown, the odds are 8 to 1 in favour of aneurysm.

CLINICAL LOCALIZATION OF THE BLEEDING POINT

Now let us look at the clinical features to see whether we can localize the bleeding point with any degree of accuracy. On careful analysis of my cases the only symptoms of any localizing value proved to be headache or facial pain. When these were unilateral the causal aneurysm was invariably discovered on the same side of the head. What of the physical signs? Forty-five per cent of the cases which I reviewed had some neurological signs, varying from an isolated cranial nerve palsy, say of the 3rd or the 6th nerve, to a dense hemiplegia or quadriplegia. A hemiplegia was present in 20%. These findings must be correlated with the fact that in my pathological material 69% of patients with ruptured aneurysms had some destruction, through bleeding, of brain tissue; of course, the incidence of intracerebral bleeding is much less in those who recover.

Such signs as high fever, hypertension, albuminuria and glycosuria are of no localizing value, but probably indicate that bleeding is severe and has irritated centres in the floor of the third ventricle. Subhyaloid hæmorrhage, too, was of no localizing value; it was often unilateral but on one occasion the causal aneurysm was on the opposite side of the circle of Willis. It is certainly not always due to a carotid aneurysm as Dandy[16] suggested. The same is true of an isolated 3rd nerve palsy—this is a common sign of an expanding supraclinoid aneurysm of the carotid artery, as is well known. However, in my series of cases, although it was sometimes produced in this way, equally often it was due to intracerebral bleeding above the tentorium with herniation of the temporal lobe, and in some cases it appeared to be due simply to direct damage to the nerve through dilatation of or bleeding from aneurysms arising from several different arteries in the suprasellar region. When this sign appears in a conscious patient with no symptoms and signs of subarachnoid hæmorrhage, it practically always indicates a supraclinoid carotid aneurysm. However, when developing after an acute episode of bleeding its significance is much more difficult to evaluate and it has little localizing value.

Focal epileptic seizures, which occurred in 3% of cases, visual field defects, indicating bleeding into the temporal lobe, and neurological signs in the extremities do, of course, lateralize the bleeding point and generally indicate accurately the site of intracerebral bleeding. On the other hand, they cannot be said to localize the aneurysm with any degree of certainty, as hæmorrhage into the frontal lobe can occur medially from the

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anterior communicating or anterior cerebral arteries, infero-laterally from the middle cerebral, or into its undersurface from the region of the carotid bifurcation. Hæmorrhage into the temporal lobe can also occur from at least three directions. It must also be remembered that a dense hemiplegia can occur in patients whose bleeding is confined to the subarachnoid space. In some such cases simple pressure of the effused blood in the subarachnoid space may be responsible, but in others (1.7% of all cases in my series) neurological signs are due not to bleeding but to coincident infarction which may be in the distribution of the artery on which the aneurysm lies or in a situation entirely remote.[17] The possibility of subdural hæmatoma, which develops in about 2% of cases of aneurysmal rupture,[18] should also be borne in mind. It is, of course, true that intracerebral bleeding and consequent neurological signs most frequently occur when the aneurysm is closely related anatomically to cerebral substance (e.g. middle cerebral and anterior communicating) and are less common when the aneurysm lies free in the subarachnoid space (e.g. internal carotid) (Table I). Again this is an observation which is valid when considering a large series of cases but is of no help in the management of an individual case.

All of these observations, based upon a detailed analysis of my cases, have led me to the conclusion that in the great majority of cases of subarachnoid hæmorrhage clinical observations are of practically no value when one is attempting to localize the bleeding point. Very rarely is it possible to do more than to indicate upon which side of the head the bleeding is occurring, and even this is often impossible. Hence, if one's scheme of management should require accurate diagnosis and localization of the causal lesion, ancillary investigations are needed. Prominent among these is cerebral angiography, which will, in a high proportion of cases, give all the information that is required. I will discuss the place of this procedure when we come to management. Very occasionally straight radiography of skull may be of some value, revealing calcification in the wall of an aneurysm or within an angioma.[19] Electroencephalography deserves brief mention. Often one finds diffuse generalized delta activity, which is of no real help. However, a delta wave focus usually indicates intracerebral bleeding in the given situation. Unfortunately this is a relatively uncommon finding. Minor degrees of lateral asymmetry of the alpha rhythm which many authors have stressed[20] seem to me to be a very tenuous basis for localization; indeed in many of the published reports the asymmetry described has appeared to be well within the limits of normal variation. I have found[21] that the electroencephalogram often reveals spikes or other focal abnormalities in patients suffering from seizures as a sequel to subarachnoid and intracerebral bleeding. I do not feel, however, that it is a dependable tool in the localization of a bleeding aneurysm, except in very occasional cases.

TABLE I.

THE INCIDENCE OF INTRACEREBRAL AND SUBARACHNOID HÆMORRHAGE RESULTING FROM RUPTURE OF ANEURYSMS IN DIFFERENT SITES

Site of aneurysm	*Intracerebral hæmorrhage*	*Hæmorrhage confined to the subarachnoid space*
Internal carotid	2	6
Carotid bifurcation	5	9
Anterior cerebral, proximal to anterior communicating	8	3
Anterior cerebral distal to anterior communicating	7	0
Anterior communicating	18	8
Anomalous anterior cerebral	2	0
Middle cerebral	33	7
Posterior communicating	5	1
Basilar	1	1
Vertebral	1	2
Posterior cerebral	1	0
Cerebellar arteries	2	1
Site not stated	0	1
Totals	85	39

PROGNOSIS

(a) *Immediate prognosis.*—In Table II, I compare the mortality rate in my series with that reported in several other published studies. The figure I give is of deaths occurring within eight

TABLE II.

THE MORTALITY RATE OF SUBARACHNOID HÆMORRHAGE

Author	*No. of cases*	*Deaths*	*Percentage*
Taylor & Whitfield (1936)	81	51	63.0
Sands (1941)	120	41	34.0
Fetter (1943)	68	27	39.0
Magee (1943)	150	84	56.0
Sahs and Keil (1943)	64	18	28.0
Wolf *et al.* (1945)	46	15	33.0
Hamby (1948)	130	67	51.5
Hyland (1950)	191	100	53.0
Ask-Upmark & Ingvar (1950)	138	38	28.0
Present series	312	140	45.0
Totals	1,300	581	44.7

weeks of the ictus. It will be seen that the proportion of fatal cases in my series, 45%, is almost identical with that obtained by collecting together 1,300 reported cases. Further analysis of the fatal cases reveals several points of interest. Ninety-one patients (66%) died in or as a result of the first attack of bleeding, whereas 47 (34%) succumbed in a recurrence of bleeding within the first eight weeks and two died of unrelated conditions. Table III gives the total

TABLE III.

DURATION OF THE ILLNESS IN THE FATAL CASES

Death in the first hæmorrhage	*Number of cases*
Within 12 hours	33
12 - 24 hours	13
1 - 2 days	3
2 - 4 days	11
4 - 7 days	12
7 - 14 days	11
over 14 days	8
Death in a recurrence	*Number of cases*
Within 1 week	7
1 - 2 weeks	22
2 - 3 weeks	8
3 - 4 weeks	6
4 - 8 weeks	4

duration of the illness in the fatal cases; those dying in a first attack are considered separately from deaths due to a recurrence. It will be seen that half the patients dying due to the first hæmorrhage did so within 24 hours, the remainder at varying times within the third to the fourteenth days. Correlation with pathological findings (Table IV) revealed that rapid death

TABLE IV.

DURATION OF FATAL ILLNESS IN PATIENTS WITH INTRACEREBRAL HÆMORRHAGE COMPARED WITH THOSE IN WHOM BLEEDING WAS CONFINED TO THE SUBARACHNOID SPACE

Duration of illness	*Intracerebral hæmorrhage*	*Confined to subarachnoid space*
0 - 24 hours	18 (46%)	8 (40%)
1 - 7 days	0	6 (30%)
7 days	21 (54%)	6 (30%)
Totals	39	20

was equally as common in patients with intracerebral hæmorrhage as in those whose bleeding was confined to the subarachnoid space. However, none of the patients with intracerebral hæmorrhage died between the second and seventh days. Hence death may be delayed by intracerebral bleeding. Another important point, which has a very considerable bearing upon management, is evident from the second half of Table III. The peak incidence of fatal recurrent bleeding was in the second week after the first hæmorrhage.

In any disease such as this, in which a fatal outcome is relatively common, attempts will be made to develop criteria which may be used for predicting the outcome in an individual case. Subarachnoid hæmorrhage is no exception to the rule, but in fact, as Richardson and Hyland[22] have pointed out, it is impossible to make such a forecast with complete accuracy. However, certain factors do exist which may be of value. Hyland[23] showed that the prognosis was worse with increasing age, Hamby[24] noted the adverse influence of recurrent bleeding, and Robertson[18] showed clearly that the outlook was worse in patients with severe neurological signs. In my own series I endeavoured to assess the significance in this connection of 80 individual symptoms, physical signs and methods of treatment. I did so by assessing the incidence of each factor in the fatal cases and in the recoveries, making corrections for possible faults in selection, such as inaccuracy or incompleteness of the history in comatose patients. The two patients who died from unrelated conditions were excluded. The incidence in the two groups was then compared by the chi-squared test and the results are given in the next three tables. Table V shows that the prognosis is undoubtedly worse with increasing age; there is a suggestion in each age group that it is worse in females, but the sex difference is certainly not significant. Table VI reveals that epileptic manifestations, loss of consciousness, an abnormal mental state, neurological signs, rapid pulse and high fever, hypertension, prolonged coma and recurrent bleeding are all unfavourable signs. On the other hand Table VII shows that the nature of the onset, a history of previous attacks occurring more than six months before the present one, papillœdema, subhyaloid hæmorrhage, glycosuria, and treatment by repeated lumbar puncture, appeared to have no influence upon the outcome. Although these results may be of some value in predicting the outcome of most cases, they are by no means infallible. All the signs may indicate a favourable outcome in a certain patient, but sudden death from catastrophic recurrent bleeding may yet occur without warning. Unfortunately we have no means of knowing in which cases this will happen.

TABLE V.

PROGNOSIS ACCORDING TO AGE AND SEX

Age in years	Deaths			Recoveries		Totals	
	Male		Female	Male	Female	Male	Female
0 - 9	1	33.0%	1	0	0	1	1
10 - 19	3		2	8	3	11	5
20 - 29	7	36.4%	5	12	10	19	15
30 - 39	9		8	16	11	25	19
40 - 49	17	43.8%	10	20	23	37	33
50 - 59	15		22	21	16	36	38
60 - 69	10	50.0%	13	11	15	21	28
70 - 79	3		11	2	3	5	14
80 - 89	0		1	0	1	0	2
Totals	65		73	90	82	155	155

TABLE VI.

FEATURES SIGNIFICANTLY RELATED MORE OFTEN TO DEATH OR TO RECOVERY

Symptom or sign	No. of cases with the feature		Significance	More frequent in
	Deaths	Recoveries		
	Total 138	Total 172		
Onset with loss of senses	40	25	Probable	Deaths
Loss of senses before admission	96	69	Probable	Deaths
Epileptic manifestations	28	17	Probable	Deaths
Coma or semicoma on admission	82	16	Very probable	Deaths
Normal mental state	3	41	Very probable	Recoveries
Pulse >100/min	17	2	Probable	Deaths
Moderate or severe hypertension	68	33	Very probable	Deaths
Abnormal neurological signs	110	21	Very probable	Deaths
Hemiplegia	37	16	Very probable	Deaths
Temp. >102°F	23	4	Very probable	Deaths
Considerable albuminuria	17	8	Possible	Deaths
Rapid improvement	11	80	Very probable	Recoveries
Recurrent bleeding	47	13	Very probable	Deaths
Coma less than 1 hour	2	31	Very probable	Recoveries
Coma 12 - 48 hours	32	13	Very probable	Deaths
Coma over 48 hours	54	14	Very probable	Deaths

(b) *Late prognosis*

Before going on to consider management, it is also important to consider what happens to those patients who recover from the illness. The results of a follow-up study of my cases were published in detail in 1952.[2] Subarachnoid hæmorrhage recurred between eight weeks and 12 years after the initial episode in 24% of my cases and in 85% of these (i.e. 20% of all survivors) the recurrence was fatal. Half of the fatal recurrences occurred in the first six months. Four patients made an incomplete recovery from the illness and died after varying intervals while another 11 died of unrelated conditions. Of the 120 surviving patients 4% were completely disabled but the remainder were able to pursue some useful activity. However, of these a third had residual symptoms which were more or less disabling, a third had relatively trivial sequelæ and only a third were symptom-free. Important sequelæ included paralytic manifestations in 10%, epilepsy in 13%, headaches in 37% (but severe only in 13%), organic mental deterioration in 9% and anxiety symptoms in 27%. These physical and mental sequelæ are similar to those of severe head injury. The study also revealed that restriction of activity after the first three months was of no value whatever in preventing recurrent bleeding. In view of these results I concluded that activity should certainly be graduated during the first few months after the illness, but after this time patients should be encouraged to live a normal life. Undue caution is valueless and may be positively harmful, resulting in severe psychoneurotic sequelæ. Confident reassurance is an essential part of rehabilitation and may even require the assertion that bleeding will not

TABLE VII.

FEATURES WHICH DID NOT OCCUR SIGNIFICANTLY MORE OFTEN IN EITHER GROUP

Symptom or sign	*Number of cases with the feature*	
	Deaths Total = 138	*Recoveries Total = 172*
Sudden onset	115	146
Gradual onset	11	13
Vomiting	75	108
Previous history of subarachnoid hæmorrhage	16	17
Papilloedema	19	21
Subhyaloid hæmorrhage	12	11
Glycosuria	9	8
More than one lumbar puncture	21	22
Repeated lumbar puncture	7	11

recur; I say this knowing full well that it does recur in over 10% of patients after the first six months, but it is far better that they should be unaware of this fact than that a lurking fear should provoke a severe anxiety neurosis. This had certainly occurred in some of the patients whom I first saw several years after the illness.

MANAGEMENT

Until recently it was commonly accepted that the essential measure in treatment of a case of subarachnoid hæmorrhage was a prolonged period of rest in bed with careful nursing and avoidance of undue physical strain. In the past the only fertile source of dispute has been the place of lumbar puncture in treatment. The advent of active surgical therapy in such cases following upon the work of Dandy,[16] Falconer,[25] Norlén,[26] Poppen,[27] Mount,[28] Hamby[29] and many others is now compelling a reorientation of opinion. The optimum role to be played by surgery is by no means clearly defined; it is a very controversial point and the most important aspect of the problem which concerns us this evening. However, this method is not yet firmly established as a method of routine management, and the comment of Wechsler and Gross[30] that "conservative treatment is a euphonious justification for doing nothing" is by no means justified. At the present time, surgical treatment is possible in only a few special centres and in the great majority of cases there is little alternative to conservative treatment. Care taken in management may pay valuable dividends and for this reason I believe we should spend a moment considering briefly the principles of conservative management.

(A) CONSERVATIVE MANAGEMENT

It is agreed that a period of strict bed rest with careful nursing and care of the bladder and bowels is essential. Many authors have suggested periods of bed rest as long as eight weeks. In my view a period of about four weeks is normally sufficient in the uncomplicated case, or two to three weeks after headache and signs of meningeal irritation have subsided. The remaining aims of treatment are firstly to relieve headache, secondly to reduce the intracranial pressure, thirdly to control excitement and epileptic seizures, and fourthly to provide adequate fluid and nourishment. It is possible that hypotensive drugs such as hexamethonium compounds of Arfonad may prove to be of some value in suppressing bleeding but these remedies have not yet been given to sufficient patients for their worth to be proven.

Many drugs have been used for headaches, but for effective relief powerful analgesics are required. In my series there was no evidence that morphine had any detrimental effect, but since this drug is known to raise the intracranial pressure, it is probably preferable to use demerol, or as it is called in England, pethidine, which does not have this effect.[31] Reduction in the intracranial pressure by mechanical means is often most effective in relieving this symptom. We have found detensifying therapy of little value in achieving this aim, though rectal magnesium sulphate can do no harm. Undoubtedly, the most efficient agent is lumbar puncture, but this procedure has its dangers, particularly when there is intracerebral hæmorrhage above the tentorium. The great risk is that of tentorial herniation; I doubt whether the removal of cerebrospinal fluid is ever responsible for recurrent bleeding. On the other hand, it is equally evident that, apart from their effect in relieving headache, repeated punctures are of no therapeutic benefit. Hence I have come to believe, as does Meadows,[15] that the procedure should be used sparingly. It is essential for diagnosis, but even this should be done with very great care, only a few drops of fluid being removed, if there is a unilateral fixed pupil or 3rd nerve palsy or other signs suggestive of a supratentorial intracerebral hæmorrhage. A narrow-gauge needle should be used to diminish the risk of persistent leakage from the puncture in the dura and arachnoid. In other cases, it is prob-

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	} 33.0%	} 50.0%					
10 - 19	3	2		8	3	11	5
20 - 29	7	5		12	10	19	15
	} 36.4%	} 38.2%					
30 - 39	9	8		16	11	25	19
40 - 49	17	10		20	23	37	33
	} 43.8%	} 45.1%					
50 - 59	15	22		21	16	36	38
60 - 69	10	13		11	15	21	28
	} 50.0%	} 57.2%					
70 - 79	3	11		2	3	5	14
80 - 89	0	1		0	1	0	2
Totals	65	73		90	82	155	155

TABLE VI.

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Normal mental state	3	41	Very probable	Recoveries
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Abnormal neurological signs	110	21	Very probable	Deaths
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Rapid improvement	11	80	Very probable	Recoveries
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Coma over 48 hours	54	14	Very probable	Deaths

(b) *Late prognosis*

Before going on to consider management, it is also important to consider what happens to those patients who recover from the illness. The results of a follow-up study of my cases were published in detail in 1952.[2] Subarachnoid hæmorrhage recurred between eight weeks and 12 years after the initial episode in 24% of my cases and in 85% of these (i.e. 20% of all survivors) the recurrence was fatal. Half of the fatal recurrences occurred in the first six months. Four patients made an incomplete recovery from the illness and died after varying intervals while another 11 died of unrelated conditions. Of the 120 surviving patients 4% were completely disabled but the remainder were able to pursue some useful activity. However, of these a third had residual symptoms which were more or less disabling, a third had relatively trivial sequelæ and only a third were symptom-free. Important sequelæ included paralytic manifestations in 10%, epilepsy in 13%, headaches in 37% (but severe only in 13%), organic mental deterioration in 9% and anxiety symptoms in 27%. These physical and mental sequelæ are similar to those of severe head injury. The study also revealed that restriction of activity after the first three months was of no value whatever in preventing recurrent bleeding. In view of these results I concluded that activity should certainly be graduated during the first few months after the illness, but after this time patients should be encouraged to live a normal life. Undue caution is valueless and may be positively harmful, resulting in severe psychoneurotic sequelæ. Confident reassurance is an essential part of rehabilitation and may even require the assertion that bleeding will not

TABLE VII.

FEATURES WHICH DID NOT OCCUR SIGNIFICANTLY MORE OFTEN IN EITHER GROUP

Symptom or sign	*Number of cases with the feature*	
	Deaths Total = 138	*Recoveries Total = 172*
Sudden onset	115	146
Gradual onset	11	13
Vomiting	75	108
Previous history of subarachnoid hæmorrhage	16	17
Papilloedema	19	21
Subhyaloid hæmorrhage	12	11
Glycosuria	9	8
More than one lumbar puncture	21	22
Repeated lumbar puncture	7	11

recur; I say this knowing full well that it does recur in over 10% of patients after the first six months, but it is far better that they should be unaware of this fact than that a lurking fear should provoke a severe anxiety neurosis. This had certainly occurred in some of the patients whom I first saw several years after the illness.

MANAGEMENT

Until recently it was commonly accepted that the essential measure in treatment of a case of subarachnoid hæmorrhage was a prolonged period of rest in bed with careful nursing and avoidance of undue physical strain. In the past the only fertile source of dispute has been the place of lumbar puncture in treatment. The advent of active surgical therapy in such cases following upon the work of Dandy,[16] Falconer,[25] Norlén,[26] Poppen,[27] Mount,[28] Hamby[29] and many others is now compelling a reorientation of opinion. The optimum role to be played by surgery is by no means clearly defined; it is a very controversial point and the most important aspect of the problem which concerns us this evening. However, this method is not yet firmly established as a method of routine management, and the comment of Wechsler and Gross[30] that "conservative treatment is a euphonious justification for doing nothing" is by no means justified. At the present time, surgical treatment is possible in only a few special centres and in the great majority of cases there is little alternative to conservative treatment. Care taken in management may pay valuable dividends and for this reason I believe we should spend a moment considering briefly the principles of conservative management.

(A) CONSERVATIVE MANAGEMENT

It is agreed that a period of strict bed rest with careful nursing and care of the bladder and bowels is essential. Many authors have suggested periods of bed rest as long as eight weeks. In my view a period of about four weeks is normally sufficient in the uncomplicated case, or two to three weeks after headache and signs of meningeal irritation have subsided. The remaining aims of treatment are firstly to relieve headache, secondly to reduce the intracranial pressure, thirdly to control excitement and epileptic seizures, and fourthly to provide adequate fluid and nourishment. It is possible that hypotensive drugs such as hexamethonium compounds of Arfonad may prove to be of some value in suppressing bleeding but these remedies have not yet been given to sufficient patients for their worth to be proven.

Many drugs have been used for headaches, but for effective relief powerful analgesics are required. In my series there was no evidence that morphine had any detrimental effect, but since this drug is known to raise the intracranial pressure, it is probably preferable to use demerol, or as it is called in England, pethidine, which does not have this effect.[31] Reduction in the intracranial pressure by mechanical means is often most effective in relieving this symptom. We have found detensifying therapy of little value in achieving this aim, though rectal magnesium sulphate can do no harm. Undoubtedly, the most efficient agent is lumbar puncture, but this procedure has its dangers, particularly when there is intracerebral hæmorrhage above the tentorium. The great risk is that of tentorial herniation; I doubt whether the removal of cerebrospinal fluid is ever responsible for recurrent bleeding. On the other hand, it is equally evident that, apart from their effect in relieving headache, repeated punctures are of no therapeutic benefit. Hence I have come to believe, as does Meadows,[15] that the procedure should be used sparingly. It is essential for diagnosis, but even this should be done with very great care, only a few drops of fluid being removed, if there is a unilateral fixed pupil or 3rd nerve palsy or other signs suggestive of a supratentorial intracerebral hæmorrhage. A narrow-gauge needle should be used to diminish the risk of persistent leakage from the puncture in the dura and arachnoid. In other cases, it is prob-

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ably justifiable to reduce the pressure to normal at the initial tap. Thereafter the procedure should be repeated only when there is continuing severe headache, restlessness, meningeal irritation, profound coma, or signs of recurrent bleeding.

The control of excitement and of epileptic seizures can be dismissed quickly. In some cases intramuscular phenobarbitone may be of value but I believe that intramuscular paraldehyde surpasses all other sedatives in such cases. So far as the provision of fluid and nourishment is concerned, it is probably wise to avoid overhydration in view of the possibility of pulmonary complications and for this reason intravenous fluid is generally contraindicated. In most patients this is rarely an important problem, since coma is of relatively brief duration. In others, fluid may have to be given rectally or subcutaneously with hyaluronidase and tube-feeding may be necessary. One must also be on the look-out for complications such as pulmonary and urinary infections. Indeed in most comatose patients it is wise to give prophylactic penicillin, and in occasional instances other antibiotics may be required.

(B) SURGICAL TREATMENT

As far as surgical treatment is concerned, I feel that it would be presumptuous to consider this in detail since most of you know far more about this question than I. However, I think it is generally accepted that two main methods are in use, namely arterial ligation and intracranial attack. The former method, though by no means free from complications, is less fraught with danger than the latter. On the other hand, it is doubtful whether carotid ligation is completely effective in the prevention of recurrent bleeding, particularly from those aneurysms which are not situated upon the carotid artery itself. So far as aneurysms upon the basilar and vertebral arteries are concerned, here surgery has very little to offer, save in rare instances. Generalizations are dangerous in considering such a subject but an increasing volume of evidence appears to suggest that, when surgical treatment is decided upon, aneurysms on the trunk of the internal carotid artery or at its bifurcation are best treated by carotid ligation, followed, where possible, by intracranial attack. For aneurysms on the anterior cerebral, anterior communicating, middle cerebral, posterior communicating and posterior cerebral arteries, intracranial operation is even more necessary, while those on the vertebral, basilar and cerebellar arteries are difficult to treat surgically with any measure of success. Carotid ligation appears to be ineffective and even dangerous in the case of angiomas;[34] these anomalies require direct attack.

(C) CONSERVATIVE TREATMENT OR SURGERY?

Finally, then, we come to the most vexed question of all—that of the indications for surgical treatment. Many neurosurgeons, notably Falconer[25] and Mount,[28] have expressed the view that all cases of this condition should be managed and treated surgically. There can be no doubt that at first sight the results and survival rates in the surgically treated series of cases reported by Dandy,[16] Jaeger,[32] Poppen,[27] Falconer[25] and Norlén[26] are infinitely better than any recorded in conservatively treated series of cases of subarachnoid hæmorrhage. But here it is essential to add a word of caution, for the comparisons made by several of these authors are by no means valid. This can best be illustrated by analysis of the figures quoted by Mount[28] in 1951. He reviewed a total of 469 cases treated surgically with a mortality of 14% and compared this figure with the mortality rate for conservative treatment which he assessed at 48%; in my series, you will remember, it was 45%. However, in Mount's surgical series intracranial aneurysms and angiomas were listed indiscriminately and many single cases were included which had probably been reported solely because of the success of surgical treatment. Even more important, a very large proportion of the aneurysms which he included were unruptured. There is no doubt that surgery within a few days of a subarachnoid hæmorrhage is much more hazardous than a "cold" operation, whatever method is used, and for this reason Mount's comparisons are valueless.

Indeed the only surgical results which can justifiably be compared with those of conservative treatment have been achieved by Falconer.[25] In 1951 he reported 69 conservative cases of subarachnoid hæmorrhage which were investigated and treated surgically. The mortality rate was 18%, and 66% of patients made a complete recovery. Even in this series there was certainly some degree of selection, since all cases were referred from physicians, some from distant hospitals an appreciable time after the ictus. As I have pointed out already (Table III), a consider-

able number of patients with subarachnoid hæmorrhage die within the first 24 hours. Such cases would never reach Falconer's unit, and it is quite possible that other methods of selection were used in collecting his cases. It is my impression that if Falconer had applied his methods of investigation and treatment to my series of cases, the results would have been far less satisfactory than those he achieved in New Zealand. Indeed, by surveying my fatal cases individually and by making an arbitrary assessment of the possible value of operation in each one, I came to the conclusion that if one excluded from consideration the possibility of complications and untoward events during surgery, the very best one could expect would be to reduce the mortality rate of the disease from 45 to about 30%. If such a result were achieved, this would be a considerable improvement upon the results of conservative treatment, though by no means as great as some surgeons would have us believe. I make this point in order to sound a word of caution, and in order to stress the fact that in my opinion the results of indiscriminate surgery in cases of subarachnoid hæmorrhage cannot at present be good enough to make surgery a *sine qua non* of treatment. Having made this point, let us now consider the pros and cons of surgical treatment to see if we can formulate some rational criteria of management.

If we take the debit side first, it is essential to consider the shortcomings of angiography, without which an informed surgical approach is impossible. To be really thorough, if no clinical indications exist as to the site of the bleeding point, one would have to take bilateral carotid and vertebral arteriograms. Carotid arteriography is not without risk, particularly in elderly, atherosclerotic individuals and in comatose subjects; it has been known to produce hemiplegia in up to 7% of patients, some of whom were relatively young and apparently in good condition.[33] The incidence of complications of vertebral angiography is considerably higher. It must also be remembered that in more than 20% of cases[13, 37] the arteriogram might fail to reveal the causal lesion, and in such cases there would be no alternative to conservative treatment. It is true that such cases with a negative arteriogram usually carry a good prognosis. In many of them the bleeding aneurysm has thrombosed and hence fails to show, while in others some pathological process more benign than aneurysm may have caused the bleeding. However, it cannot be assumed that all patients with negative arteriograms recover. Another point worth making is that in my autopsy series of 145 intracranial aneurysms, 15% were situated on the vertebral-basilar system of vessels; in this situation effective surgery is often very difficult. Only 25% were upon the internal carotid artery at its bifurcation, while 30% arose from the middle cerebral artery in the Sylvian fissure and another 28% from the anterior communicating. Surgical treatment is most satisfactory in the case of carotid aneurysms and is much more difficult in the other two situations. It must also be remembered that in the cases of unusual etiology, surgical treatment would be impossible in some and would require a different approach in others, particularly those harbouring intracranial neoplasms. So far as angiomas are concerned, much the same problems apply as in the case of aneurysms; some can be excised,[34] others are too extensive for surgery.[35] Finally, it cannot be denied that surgical methods carry considerable hazards. Even carotid ligation may be followed by hemiplegia in about 8% of cases[27, 36] while any operation upon intracranial structures involves a substantial risk. These risks are far greater in ill or comatose patients who have bled recently.

Now what of the credit side? Firstly, it is clear from the figures I have quoted that a distinct improvement upon the immediate results of conservative treatment is possible with effective surgery. More important still is the probability that surgical measures would prevent most of those fatal recurrences of bleeding which frequently occur in the second week after the ictus, as well as fatal recurrent bleeding after a substantial interval, as occurred in 20% of my cases. Furthermore, increasing experience with carotid arteriography has shown that in experienced hands the procedure has increasingly few complications, except in elderly, hypertensive and atherosclerotic patients. Surgical technique is improving rapidly and the use of hypotensive drugs has greatly diminished the dangers of operation. As I pointed out earlier, there are many clinical signs which suggest a favourable prognosis in subarachnoid hæmorrhage; in my series 90% of patients under the age of 40, with no severe alteration of the sensorium, normal blood pressure and no neurological signs, recovered. However,

in the remaining 10% unpredictable and catastrophic bleeding recurred. It seems to me that the only possible way in which such tragedies can be averted is by the judicious application of surgical methods of treatment. Indeed this is probably the only way in which one can hope to reduce the mortality of the disease.

However, it is important to stress once more that indiscriminate surgery is likely to bring the method into disrepute, and for this reason the exercise of clinical judgment and careful selection of cases is essential. In order to achieve this aim it is essential to have as much information as possible, and for this reason I feel that angiography is indicated as a routine measure in such patients unless there are very real contraindications. Certainly it is doubtful if surgery could ever save patients dying within 24 hours of the ictus or even in the first two or three days, but in individuals who survive this period I feel that bilateral carotid arteriography should be done. I say bilateral because of the appreciable number of patients who have multiple vascular anomalies.[37] Not only will this reveal in many cases the situation and nature of the lesion causing bleeding, but it may also indicate the presence of other complications such as intracerebral or subdural hæmatoma which may require surgical treatment in their own right. If the arteriograms are negative, there will be no satisfactory alternative to conservative treatment. I do not feel that it is profitable to proceed to vertebral angiography in the average case, in view of the high incidence of complications of this procedure and since aneurysms lying upon this system are rarely amenable to surgery. If, however, an aneurysm or angioma is revealed, this is the time when consultation between physician and surgeon is of paramount importance. Each individual case deserves careful consideration and a plan of management should be formulated depending upon the site, size and nature of the bleeding anomaly, and the age and condition of the patient. In some cases where the aneurysm is large and accessible, surgery may be clearly indicated; in others, when all clinical pointers suggest a favourable outcome, or when the aneurysm or angioma will clearly prove difficult to treat effectively, it is probably preferable to temporize. Being possessed of all relevant information, the surgeon is in a position to operate should the patient's condition deteriorate or recurrent bleeding occur. In Table VIII I have collected figures showing clearly that the patient's chance of survival with conservative treatment increases steadily with passage of time after the initial bleeding. The two danger periods are the first 24 hours, when surgery is unlikely to help, and the second week of the illness. It follows that if operation is decided upon, this should preferably be done within the first ten days of the illness, since so many recurrent hæmorrhages occur during the second week. When the second week has passed, the advantages to be gained by surgical treatment, unless the aneurysm is very favourably situated, become progressively less with the passage of time. Should a patient be first seen four weeks or more after the ictus, conservative treatment is generally advisable unless there is clear evidence of inadequate recovery from the bleeding, persisting intracerebral hæmorrhage, subdural hæmatoma or aneurysmal dilatation. In certain cases, of course, operation will be required in the subsequent weeks and months when there are signs to indicate enlargement of the aneurysm or angioma. However, in general, a patient who is seen some six months or more

TABLE VIII.

THE MORTALITY RATE IN PATIENTS WITH SUBARACHNOID HÆMORRHAGE AT DIFFERENT INTERVALS AFTER THE ICTUS

Time after the ictus	*Total surviving patients*	*Died later as a result of the first hæmorrhage*	*Died later of recurrent bleeding*		*Survived period of follow-up*
			Recurrence within 8 weeks	*Late recurrent bleeding*	
24 hours	264	45 (17%)	41 (18%)	35 (13%) Total 82 (31%)	137 (52%)
1 week	231	19 (8%)	40 (17%)	35 (15%) Total 75 (32%)	137 (60%)
2 weeks	198	8 (4%)	18 (9%)	35 (18%) Total 53 (27%)	137 (69%)
4 weeks	176	—	4 (2%)	35 (20%) Total 39 (22%)	137 (78%)
6 months	154	—	—	17 (11%)	137 (89%)

after complete recovery from a subarachnoid hæmorrhage does not require investigation or consideration of surgery, for at this time the combined risk of angiography and operation is just as great as that of fatal recurrent bleeding.

From the evidence I have presented to you, one must conclude that we have as yet no absolutely clear-cut criteria to indicate the place of surgery in the treatment of patients with this disease. I do hope, however, that I have managed to convey to you my feeling that this condition is one in which the utmost co-operation and consultation between neurologist and neurosurgeon will undoubtedly pay dividends. I am confident that such a liaison, together with improvements in surgical and anæsthetic techniques, will eventually lead to a substantial reduction in the mortality of the disease.

I am grateful to Professor F. J. Nattrass and to the physicians of the Royal Victoria Infirmary, Newcastle upon Tyne, England, for permission to report information derived from patients who were under their care. I also wish to thank Professor J. B. Duguid for allowing me to review the pathological material and Mr. H. Campbell of the Department of Industrial Health, King's College, for help with the statistical aspects of the investigation.

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APPENDICITIS—A REPORT OF TWO SEVEN-YEAR SURVEYS

BURNS PLEWES, M.S., F.R.C.S., and L. TESKEY, Jr., M.D., *Toronto*

THE MORTALITY from appendicitis has been reduced to two deaths per 1,000 cases from 26 per 1,000 fifteen years ago. This is shown by a survey of all appendectomies at the Toronto East General Hospital during the years 1946-1952 inclusive as compared with a similar study of the 1933-1939 period. In each series the same classification was used, cases being divided into three main groups: (1) acute, (2) chronic and (3) incidental. Acute appendicitis was divided into unruptured and ruptured. "Chronic appendicitis" included cases which were considered acute by the surgeon but reported otherwise by the pathologist.

During the interval between 1939 and 1946 many changes occurred both in the field of medicine generally and in the Toronto East General Hospital. Antibiotics, a clearer understanding of fluid and electrolyte balance, improved anæsthesia and early ambulation were great advances in treatment. At this hospital, the restriction of surgical and anæsthetic privileges to specialists and improved postgraduate and residency training especially contributed to the better care of surgical patients.

The overall reduction in the mortality of appendicitis is shown in Table I. In the "thirties" patients with acute appendicitis had a 95 out of 100 chance of surviving while in the "forties" such a patient had a 99.7% chance of recovery. The removal of the uninflamed appendix showed a mortality rate of nearly 1% in the first series and one-tenth of 1% in the second. Those subjected to appendectomy during other surgi-

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cal procedures also had a ten times better chance of survival in the later series. The overall mortality of appendectomy was lowered from 2.57 to 0.19%.

Acute appendicitis is more closely reviewed in Table II. If the inflamed appendix was not ruptured, treatment was followed by 6 deaths in 537 cases in the first series and 3 deaths in 1,608 cases in the second. More spectacular was the reduction from 30 deaths in 191 cases of ruptured appendicitis to 3 deaths in 287 cases, improving the chance of survival from 85 to 99 chances in a hundred. Nevertheless, if acute appendicitis goes on to peritonitis, the patient is still subjected to a six-fold increase in mortality rate and twice the length of hospital stay.

"Chronic appendicitis" is a term used to classify those appendices removed as clinically acute or recurrent but which the pathologist reported as "normal," "pinworms," "fibrosis," "fæcolith," "healing" or the unqualified "appendix." In Table III this group is subdivided into: (a) those in which the clinical diagnosis of acute appendicitis was not concurred in by the pathological department and (b) those diagnosed clinically as "interval," "recurrent" or "chronic" appendicitis with appropriate pathological confirmation. The death rate following appendectomy when the appendix is not acutely inflamed has dropped from 1 in 100 to 1 in 1,000 cases. "Chronic" and "interval" appendectomies resulted in no deaths in 1946-1952. The clinically acute group (2a), while showing a reduction of ten times in mortality rate, also shows an increase from 14.7 to 24.5% of the total number of appendectomies.

It seems evident that the increasing safety of operations in uncomplicated or doubtful appendicitis has resulted in more frequent appendectomies rather than continued observation and delay. The decreased incidence of ruptured appendicitis in the recent series may be the result. It is suggested that it would be safer for patients if early appendectomy were performed in doubtful cases of "acute abdomen" than if the surgeon continued to boast that he never removes a normal appendix.

Antibiotics have undoubtedly had a great deal

TABLE I.

APPENDECTOMIES

	1933 - 1939			*1946 - 1952*		
	Total	*Deaths*	*%*	*Total*	*Deaths*	*%*
Acute	728	36	5.0	1,895	6	0.31
Chronic	954	9	0.94	2,258	2	0.09
Incidental	419	9	2.14	1,160	2	0.17
Total	2,101	54	2.57	5,313	10	0.19

TABLE II.

ACUTE APPENDICITIS

	1933 - 1939			*1946 - 1952*		
	Total	*Deaths*	*%*	*Total*	*Deaths*	*%*
Unruptured	537	6	1.1	1,608	3	0.18
Ruptured	191	30	15.7	287	3	1.04
Total	728	36	5.0	1,895	6	0.31

TABLE III.

CHRONIC APPENDICITIS

	1933 - 1939			*1946 - 1952*		
	Total	*Deaths*	*%*	*Total*	*Deaths*	*%*
Clinically acute; pathologically not acute	310	4	1.3	1,304	2	0.15
Clinically chronic; pathologically chronic	644	5	0.78	954	0	0.0
Total chronic	954	9	0.94	2,258	2	0.09

TABLE IV.

ANTIBIOTICS IN ACUTE APPENDICITIS

	1946	*1947*	*1948*	*1949*	*1950*	*1951*	*1952*
Cases of acute unruptured appendicitis	108	189	237	270	256	256	299
Antibiotics %	19.4	33	37	49	50	70	70
Average hospital stay in days	7½	7	7	6½	6	6	6½
Cases of ruptured appendicitis	29	47	40	36	49	43	43
Antibiotics %	100	91	95	89	100	100	100
Average hospital stay in days	16	12	16	15	14½	12½	13

to do with the decreasing mortality from acute appendicitis. Yet, as seen in Table IV, there has been no statistically demonstrable decrease in hospital stay for patients with either ruptured or unruptured appendicitis during the years 1946-52. The sulphonamides and penicillin were available and were used for sick patients in 1946. In 1948 streptomycin appeared. From this time the popularity of sulphonamides waned and other antibiotics became available, but penicillin and streptomycin alone or in combination were by far the most frequently employed.

In this series of 5,313 appendectomies, mesenteric adenitis was recorded in 48 cases, pinworms in 41, Meckel's diverticulum in 19 (one case of acute Meckel's diverticulitis), and carcinoid tumour of the appendix in 17. In six cases diagnosed preoperatively as acute appendicitis, ectopic pregnancies were found. There were 25 cases of ectopic pregnancy which were also subjected to appendectomy.

The ten deaths are summarized in Table V. The cause of death listed is that given on the death certificate; the terms in parentheses show the cause of death which would probably be more accurate in the light of present knowledge. Study of the case histories led to the conclusion that 7 out of the 10 patients died of other causes than appendicitis or its sequelæ although all but one (No. 10) had clinical signs and symptoms of acute appendicitis. In retrospect, 3 patients (Nos. 5, 9 and 10) did not require appendectomy. Another three died as a result of operation rather than of the lesion present (Nos. 1, 3 and perhaps 8). In 2 cases (Nos. 2 and 5) death was not due to disease of the appendix but was attributed to heart disease. Two died of pulmonary embolism (Nos. 6 and 7) when apparently

TABLE V.

DEATHS

No.	*Year*	*Age*	*Clinical diagnosis*	*Pathology (appendix)*	*Surgical findings*	*Time of death*	*Cause of death*
1	46	51	Acute	Acute	Acute	O.R.	Coronary occlusion; Spinal anæsthesia; (Cardiac arrest)
2	46	74	Acute	Fibrosis	Subphrenic abscess	3rd day	Toxæmia; Myocardial degeneration
3	47	17	Acute	Acute	Acute	O.R.	Spinal shock; Spinal anæsthesia; (Cardiac arrest) Autopsy
4	47	67	Acute	Acute	Ruptured	9th day	Acute appendicitis, perforated; Peritonitis
5	47	73	Acute	Chronic	Acute	7th day	Coronary sclerosis
6	48	57	Acute	Acute	Ruptured	3rd day	Pulmonary embolus
7	49	61	Acute	Acute	Ruptured	10th day	Pulmonary embolus
8	49	65	Acute	Acute	Acute	4th day	Retroperitoneal hæmatoma; Cerebral thrombosis; Autopsy
9	50	39	Acute	Periappendicitis	Acute	6th day	Fatty liver, atelectasis; Wound disruption; Autopsy
10	52	44	Chronic cholecystitis	Fæcolith	Chronic	4 hours P.O.	Coronary thrombosis

recovering from ruptured appendicitis. Only one (No. 4) died of peritonitis. Three only (Nos. 4, 6, 7) can be said to have died of appendicitis. It is suggested that 3 out of the 10 deaths (Nos. 2, 5, 9) were related to mistaken preoperative diagnosis. It was noted that none of the deaths occurred among public ward patients.

A decrease of 10% in the number of ruptured appendicitis cases, and an increase of 10% in the number of clinically acute ones not confirmed by pathological examination, may indicate a trend toward earlier diagnosis and treatment. It would be a retrogressive step if newly formed Tissue Committees were severe in their criticism of the appendectomy which is proved unnecessary by the pathologist's report of "normal appendix". A proportion of such operations seems indicated if the increased mortality from perforated appendicitis is to be avoided. This is an admission of imperfections in the art of differential diagnosis of the acute abdomen which few if any experienced clinicians contradict.

CONCLUSIONS

1. Studies of appendectomies at the Toronto East General Hospital before and after the recent war show a ten-fold reduction in the mortality rate. Ruptured appendicitis has become fifteen times less fatal.

2. Many factors are suggested as having effected this improvement. Chemotherapeutic and antibiotic agents are probably the most important of these.

3. In the postwar period there was a 10% increase in appendectomies for "clinically acute but unconfirmed pathologically" cases. At the same time there was a 10% decrease in the incidence of ruptured appendicitis.

4. Ten deaths occurred in the more than 5,000 cases in the postwar period. Only three deaths were directly due to appendicitis or its sequelæ.

5. The mortality of appendicitis may be further reduced if the present trend toward earlier operation is continued, with greater attention to the art of differential diagnosis.

6. The treatment of acute appendicitis is immediate appendectomy.

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RÉSUMÉ

D'après les statistiques du Toronto East General Hospital, la mortalité de l'appendicectomie dans les années 1946-1952 est dix fois plus basse qu'elle ne l'était dans la période de 1933-1939. La mortalité due à l'appendicite avec péritonite a de même diminué de quinze fois ce qu'elle était. Parmi les nombreux facteurs qui ont contribué à cette amélioration, la chimiothérapie et les antibiotiques viennent au premier rang. Les années d'après Guerre ont vu une fréquence accrue de 10% dans les appendicites cliniquement aiguës sans confirmation anatomo-pathologique. Concurremment, il y eut une baisse de 10% dans la fréquence des appendicites suppurées. Dans cette même période, il n'y eut que 10 décès pour 5000 interventions, et trois seulement furent le résultat direct de l'appendicite et de ses suites. La mortalité de l'appendicite peut être diminuée davantage si la tendance actuelle vers le lever précoce est maintenue, et si une plus grande attention est apportée au diagnostic différentiel. Le traitement de l'appendicite aiguë est l'appendicectomie immédiate. M.R.D.

THE R.C.A.M.C. IN THE KOREAN WAR*

BRIGADIER K. A. HUNTER, O.B.E., C.D., M.D., Q.H.P.† and
COLONEL J. E. ANDREW, E.D., B.A., M.D., C.M., F.R.C.S.(Ed.), F.R.C.S.[C.],‡
Ottawa

SUBSEQUENT to the 1939-45 War, the Canadian Regular Army was reorganized on a structural basis which provided for a small, compact, highly efficient force which in turn would be capable of rapid and large expansion should the occasion demand. Included in this Regular Army were elements which would provide for the administration and training of the Canadian Reserve Army, which in turn continued to be considered the central means for providing the very large army which Canada would require in case of a large-scale international conflict. In addition, in the Regular Army there was organized a mobile striking force of regulars designed to be the first line of defence in case of attack being mounted against Canada across the northland areas.

Within the structure of this small regular army the R.C.A.M.C. was reorganized in 1946-47. The Royal Canadian Army Medical Corps, like the Regular Army, was small, compact and highly efficient for its purpose. The purpose of

*Read at the meeting of the Armed Forces Medical Section of the Canadian Medical Association, Vancouver, June 1954.
†D.G.M.S., Canadian Army.
‡Professional Adviser to D.G.M.S.

the R.C.A.M.C. as well as the Regular Army, it will be remembered, was the provision of training and administration for the Reserve Army and the provision of a mobile striking force which would be Canada's first line of defence in case of attack on Canada itself. During the period 1946 to 1950 the R.C.A.M.C. grew within this structural framework. The various tasks assigned to the R.C.A.M.C. were accepted and fulfilled during this period.

During the summer of 1950 the North Korean communist aggression against the South Korean Republic resulted in a world-wide reaction. The United Nations organization found ways and means of negating the effectiveness of the vetoes wielded by the U.S.S.R., and the U.N. Security Council called upon the member nations to provide forces and arms for the support of the victim South Korean Republic. The U.S. Armed Forces were thrown into battle at once and the other member nations of the U.N. made preparations to assist in the war against the aggressors.

Canada, being a member nation in the United Nations organization, was faced with a decision in this regard. The government of Canada accepted the responsibility devolving upon Canada as a member nation of the United Nations organization and took steps toward the production of forces for the Korea "police action." It was decided that Canada would provide an Army Brigade Group as well as certain Royal Canadian Air Force and Royal Canadian Naval operational elements.

Since the small Canadian Regular Army was not designed to provide for overseas forces, it was necessary to organize a new formation, namely, the 25th Canadian Infantry Brigade Group, for the purpose of taking the field in Korea alongside the other forces of the United Nations. Special recruiting drives were held in August 1950. The new brigade group, 25th Canadian Infantry Brigade, was recruited and began training during the autumn of 1950.

An independent Army Brigade Group, in Canadian organization, ordinarily includes three Infantry Battalions, one Artillery Regiment, an Army Service Corps Supply and Vehicle Unit, an Ordnance Supply Unit, and elements of the Royal Canadian Signals, Royal Canadian Engineers, and Royal Canadian Armoured Corps. In addition, a Royal Canadian Army Medical Corps Unit, namely a Field Ambulance, is usually included in the establishment of such an independent Brigade Group. In the case of the newly formed Brigade Group the normal structure was maintained and a new Royal Canadian Army Medical Corps unit was recruited and organized for duty with this Brigade. This unit was the 25th Canadian Field Ambulance. It may be said at this point that in addition to the Field Ambulance there are included within a Brigade Group certain other medical elements which are part and parcel of the fighting units. The R.C.A.M.C. elements in the combatant units are the medical officer, who is an R.C.A.M.C. officer attached to the Infantry or Artillery, and five non-commissioned officers of the Royal Canadian Army Medical Corps who are attached to each combatant unit.

During the autumn and winter of 1950-51, 25th Canadian Infantry Brigade Group and the R.C.A.M.C. units and elements which were part of that Brigade Group were trained and prepared for despatch to the Far East.

In the spring of 1951, two senior officers of the R.C.A.M.C. were despatched to the Far East to examine and make an appreciation of the situation as regards medical arrangements for the Canadian Infantry Brigade Group when that formation would be despatched to the theatre of operations. At about the same time it became apparent that the Canadian Infantry Brigade Group would probably not be operating as an independent Brigade Group but would more probably become part of a Commonwealth Division, which would in turn consist of three Brigade Groups provided by Commonwealth countries and, in addition, Divisional supporting troops for these fighting Brigades.

Originally it had been considered that the independent Canadian Brigade Group would be operating alongside United States Army formations and would make use of the supply, medical, transportation and other organizations which were part of the large American Army operating in the Korean theatre. In so far as the medical contribution by Canada was concerned this concept had been, up to that time, a legislating factor and it had not been considered necessary to provide medical units from Canada other than those which were the normal complement of an independent Brigade Group.

The formation of the Commonwealth Division presented the Commonwealth authorities with the problem of providing a Field Dressing Station to round out the divisional medical organization. A Field Dressing Station is capable of providing a firm base for the operations of surgical teams and transfusion teams, thus providing what is, in effect, a small hospital for the definitive care of wounded soldiers.

The investigating officers on examining the situation in Korea and Japan found that the U.S. Army had already made provision for field hospitals near the battle line, and along the lines of communication back to Pusan, which is a sea port lying at the southern extremity of the Korean peninsula. In addition, in Japan some 500 miles by air from the battle line, a combined British and Australian hospital was established

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and operating at Kure. It was found also that the Royal Australian Air Force was prepared to provide transportation for casualties from airdromes close to the battle line back to the Commonwealth hospital area in Japan.

In the immediate battle area the United States Army Medical Service had established Mobile Army Surgical Hospitals for the purpose of providing immediate surgical care for casualties of all types. In addition, the U.S. medical authorities were providing helicopters for the evacuation of casualties from the front line to the Mobile Army Surgical Hospitals.

From an examination of the situation, it was apparent that the U.S. Army medical authorities and the Commonwealth authorities were in a position to provide adequate medical attention for all Canadian casualties after those casualties had been evacuated from the battle lines. Normal plans for the Canadian Infantry Brigade Group were such as to provide the early care for the wounded, and evacuation from the battle lines, by R.C.A.M.C. personnel of the Canadian Field Ambulance.

Throughout the two Great Wars, in which Canada has played a large part, it has been the policy of the Canadian Army to provide Canadian medical attention for Canadian casualties at all levels where such attention is necessitated. This policy has been based on the fact that the Canadian soldier expects treatment by Canadian doctors and nurses whenever it is possible to provide such treatment. This policy does not cast a reflection upon the professional ability of doctors and nurses other than those of Canadian origin but rather is based on a sentimental and natural desire of the wounded man for contact with people from his own homeland.

Bearing all factors in mind, investigating officers proposed certain additions to the Canadian medical contribution to the Far East theatre. The organization, as proposed and put into effect, was as follows:

(a) The 25th Canadian Field Ambulance and the Regimental Medical establishments would provide the initial first-aid treatment and evacuation of casualties to hospitals in or near the battle area.

(b) 25th Canadian Field Dressing Station would be organized and despatched to the Far East to act as the Divisional hospital for the Commonwealth Division.

(c) A Field Surgical Team and a Field Transfusion Team were to be organized and despatched for duty with the 1st British Commonwealth Division.

(d) At Kure, Japan, the British Commonwealth General Hospital was to be supplemented by a Canadian Section consisting of three medical officers, seven nursing sisters and 21 non-commissioned officers and men of the Royal Canadian Army Medical Corps.

Since all Canadian casualties were to be collected at Seoul, Korea, for despatch by air to the Commonwealth General Hospital at Kure, Japan, it will be apparent that, by providing the units enumerated herein, provision was being made for Canadian medical personnel to be available for the care of Canadian casualties at all levels from the time of wounding until the casualty had reached the base hospital in Japan. From the base hospital in Japan, if the casualties were to be evacuated to Canada as unfit for further service, such evacuation to Canada was to be carried out by the American Air Force Medical Service.

The Canadian Infantry Brigade Group sailed for Korea in April 1951. Accompanying it were 25th Canadian Field Ambulance plus the Canadian Field Surgical Team and the Canadian Transfusion Team. In the following July the 25th Canadian Field Dressing Station proceeded to Korea and was available for duty by August. Throughout the balance of 1951 and the year 1952 Canadian medical units and components applied themselves to their appointed task and, in spite of many difficulties and privations, provided a very high level of medical and surgical attention for the Canadian soldiers fighting in Korea. In addition to the thousands of Canadian casualties who passed through the Canadian medical units, there were additional thousands of Commonwealth and U.S. Army casualties who received care and attention at the hands of the R.C.A.M.C. personnel. It will be appreciated that in addition to the Canadian medical effort there was a concomitant effort by British, Australian and American medical units. Medical units of the United Nations all worked together to provide best possible medical and surgical care for all soldiers, no matter from which nation they might have come.

Early in 1953, as a result of further investigations by a senior Canadian medical officer, it was decided that some further Canadian contribution to the medical services of the Commonwealth fighting in Korea might be made. By this time the Canadian Field Dressing Station had become, in effect, a small field general hospital operating in the area of the Commonwealth Division. Considerable surgical attention was being given to casualties within 15 miles of the

battle line. Provision of this attention resulted in the early recovery of the wounded and sick and their consequent return to duty with their units without the delay which would be consequent upon the evacuation of such casualties a distance of 500 miles to Japan. In order to make this small hospital work at the highest level of efficiency, it was considered that nursing sisters should be provided for the postoperative care of casualties. As a result an additional detachment of Royal Canadian Army Medical Corps Nursing Sisters was despatched to Korea for duty at the Field Dressing Station.

In addition to the care of the sick and wounded soldiers of the Commonwealth and United Nations Forces, the Royal Canadian Army Medical Corps made a further contribution to the United Nations' effort by providing, to as great an extent as possible, medical care for the local Korean population. It is considered that this gesture will enhance markedly the reputation of Canada among the unfortunate South Korean people.

MEDICAL PROBLEMS AND CASUALTY MANAGEMENT

The interval between the Second World War and the Korean conflict was sufficiently short for the lessons learned in the fields of war medicine and surgery not to have been forgotten. Unfortunately, many of the medical personnel were without actual medical experience in a theatre of operations. But under guidance these personnel applied the old accepted principles and helped to develop new practices and procedures. The problems encountered in Korea were those of modern war fought with conventional weapons, a largely mountainous terrain almost devoid of roads, a climate varying from heavy rain followed by heat and dust in summer to the extreme cold of winter, and the prevalence of diseases endemic in the country. How well these problems were met is reflected in the low mortality rate from disease and wounding (Table I).

Among the diseases encountered in Korea was the little-known hæmorrhagic fever, described to some extent by the Japanese in 1939. This condition is an acute febrile illness with increased capillary permeability, hæmorrhagic tendencies, hypotension and renal damage. Cases varied in severity from mild to those requiring treatment for shock. Usually there were a febrile phase, a hypotensive and oliguric phase, and a diuretic phase. The cause of the disease has been difficult to determine but is now generally considered to be a virus, with the vector a chigger mite associated with rodents. Preventive measures have been directed to the eradication of rodents and the impregnation of clothing with miticidal and repellant materials. The treatment is non-specific, consisting chiefly of carefully controlled physiological support. As cases travelled poorly by road, helicopter evacuation was used when feasible and was believed to reduce hæmorrhage and shock. It was found best to centralize such cases for the benefit of experience in evaluation and therapy. The mortality rate among United Nations troops was 5 to 7%.

TABLE I.

Campaign	*Mortality rate of wounded per 1000 wounded*	*Mortality rate from disease per 1000 soldiers per annum*
Boer War (British).....	93	22.0
World War I (Canadian).....	114	6.0
World War II (Canadian)....	66	0.9
Korea (Canadian).....	34	0.7

Malaria is prevalent in Korea but the incidence of primary attacks among our troops in the Far East was not high and lessened with experience. Paludrine was used as the suppressive drug by the Canadian Forces. However, following the rotation of the Canadian Brigade in 1952, over 1,000 cases of malaria were reported during the next several months in Canada. It was decided to treat these "breakthrough" cases with primaquine plus quinine or chloroquin. With this therapy there were few recurrences. It was also decided that as troops left the Far East theatre they would be given a 14-day course of primaquine in an attempt to destroy the tissue forms of the parasite. The Brigade returning to Canada in 1953 had only one-fifth of its predecessor's malaria incidence.

Venereal disease has a high incidence in the Far East and one must admit that our Canadian rates were high also. However, the number of man days lost due to V.D. was relatively small, as our policy has been to treat these cases on an ambulatory basis. Very few require hospitalization. Syphilis has been fortunately rare, chancroid more common, but mostly the infections have been gonococcal or non-specific urethritis.

Jaundice due to infectious hepatitis occurred but never reached serious proportions. Homologous serum jaundice cases were encountered and apparently were due to infected plasma infusions.

During the period of active hostilities in Korea the Divisional Psychiatrist for the 1st Commonwealth Division was supplied by the R.C.A.M.C. This officer was stationed at the Field Dressing Station where he maintained a small ward for observation cases and short-term treatment. The general policy of treatment as close to the front as possible was being maintained in order to minimize the factor of gain through illness. The psychiatrist visited regularly the Field Ambulance where the patients were sent. Those with slight or no disability were returned directly to duty. Cases of more severe disability were kept at the Field Dressing Station for short-term psychotherapy and sedation, the majority either being returned to their units or employed in rear areas in Korea. The cases medically evacuated from Korea consisted of psychosis and severe psychoneurosis such as intractable conversion reactions. Psychoneurosis occurred at the rate of two per thousand per annum; this is the rate to be expected in any comparable group of people. Battle exhaustion did not occur to any great extent, due, it is felt, to the nature of the fighting in which battles were of short duration and the fatigue factor was not operative. Psychiatric consultation was frequently requested in the case of soldiers accused of breaches of discipline. These cases were examined and, if no medical disability was present, were returned to their units for administrative disposal.

As there was only one Canadian Field Surgical Team in Korea, and in the early days it was based on an American Mobile Army Surgical Hospital (MASH), part of the initial or forward surgery was performed by American and to some extent by Norwegian surgeons. As soon as it was possible, these casualties were returned to Canadian channels. Further hospitalization and surgery, as required, was carried out at the British Commonwealth Hospital in Kure, Japan, where there was a Canadian section.

The lowering of mortality rates in Korea was due to a number of factors: helicopter evacuation, armoured vests, more abundant and varied antibiotics and improvement in resuscitation and the treatment of impending or established renal shut-down.

Resuscitation measures were noteworthy for the large amounts of whole blood frequently employed and for the introduction of plasma volume expanders. Plastic disposable intravenous equipment was used in Korea and reactions which might be attributed to the set were noticeably absent. This was not the case in the British Commonwealth Hospital in Japan where recoverable rubber sets were employed. It was appreciated that wound shock is due chiefly to a deficiency of circulating blood in the arterial system, and efforts were made to correct this deficiency quickly and adequately. Intra-arterial blood transfusion was frequently used in cases of profound shock, and in selected cases was considered to be more beneficial than multiple transfusions by the intravenous route. Recent investigations indicate, however, that the rate of transfusion and not the route is the important factor. Group "O" low titre blood, if possible no more than 14 days old, was used in the forward areas and was ordinarily in abundant supply. Very large amounts of blood were administered in certain serious casualties, sometimes with success but, as might be expected, mortality rates were higher when large quantities were required. The following U.S. figures for the blood requirements for 1,000 Korean casualties during the first 24 hours are interesting:

TABLE II.

Blood used	*No. of casualties*	*% of casualties*	*Mortality*
0 - 4 pints.....	862	86%	1%
5 - 14 pints.....	111	11%	8%
15 or more.....	27	3%	41%

The Korean conflict was essentially a small-scale war for which abundant services and supplies could be provided. This desirable situation would present a serious problem in a large-scale war.

The plasma volume expander, dextran, was used considerably in resuscitation in the forward areas with generally satisfactory results. It was, of course, no substitute for blood but was useful for increasing the circulating blood mass. Dextran was used where plasma was normally administered or where blood was not available. It eventually supplanted plasma when it was discovered by U.S. Medical Corps follow-up that more than 20% of their patients who had re-

ceived pooled plasma went on to develop homologous serum jaundice.

The value of good anæsthesia and the need for skilled anæsthetists was again demonstrated in Korea. Canadian equipment was good and our anæsthetists were able to play their full part in the repair teams. Cyclopropane was made available and was frequently the anæsthetic of choice among Canadians. The anæsthetists did much to spread the gospel of intravenous administration of morphine in the forward areas. The danger of the cumulative effect of repeated subcutaneous or intramuscular doses of morphine in the shocked patient was stressed. The old Army custom of providing the casualty with innumerable cups of hot, sweet tea or other beverages as he passed down the evacuation line to surgery was also decried by the anæsthetists.

Surgical practices in the management of wounds were much as they were in 1945. The same adequate débridements and the "no suture" techniques were employed. Plentiful antibiotics might improve results but were no substitute for thorough, early, initial surgery. It is not within the scope of this paper to attempt detailed descriptions of the treatment of individual types of injury. A few comments are offered only where there may have been a change in policy.

In certain instances abdominal cases were evacuated by air to Japan on the 6th or 7th postoperative day perhaps because of local bed requirements. Air evacuation usually results in some abdominal distension, an ambulance ride is associated and considerable handling of the patient is required. Most patients arrived distressed and there were some wound disruptions. This served to emphasize that the normal policy of holding abdominal cases for 10 days after operation is sound.

Chest wounds were handled ordinarily by the conservative measures of closure and aspiration unless formal thoracotomy was indicated for continued profuse hæmorrhage or injury to other intrathoracic organs. However, in cases going on to empyema the value of early decortication in 3 to 5 weeks was recognized and practised. Many lung fixations were thus corrected and many patients restored to duty.

Burns, chiefly due to accidents, were fairly common, particularly in the winter months. Fluid (including blood) requirements were restored, burn toilets were carried out and occlusive dressings applied. The large N.R.C. special burn dressings were employed to some extent as first-aid measures and also after local treatment. The value of the open or exposure method of burn treatment was appreciated, but it was not found to be practical when patients had to be evacuated after débridement. Minor burns on patients held in forward areas could be left open and many burns originally dressed in Korea were exposed some three to five days later in Japan with good results.

The Tobruk splint, so familiar to Canadian medical officers, especially in the Spaghetti League, was replaced by the hip spica in the treatment of fractures of the femur. Likewise, amputations tended to be of the circular type with applied traction. This was American policy.

The problem of the early repair of important arterial lesions in battle casualties was studied, and methods were demonstrated by American specialists in this field. With improved techniques and patient management, many successful repairs were carried out where ligation only would have been done in World War II. The need for early recognition of the lesion, splinting of the limb, control of hæmorrhage by dressings rather than by tourniquet and early evacuation to the surgical centre was emphasized. All forward surgeons should be familiar with arterial repair, although time might not allow for more than ligation if casualties were extremely heavy. The Korean studies in vascular surgery have been well worth while.

American shock research teams went to Korea in 1952 to study the problems associated with resuscitation and renal shut-down. Intensive investigations and therapeutic measures included dialysis with an artificial kidney. Much knowledge of the problem was gained and the artificial kidney saved some lives. A number of our Canadian officers had the opportunity of visiting this centre and a few were attached for a valuable period. We are grateful that the larger American medical services in Korea were able to undertake this important research and shared their valuable experience and knowledge. While artificial kidney units, as such, may not be altogether practical in another major war, the knowledge gained will make for a better management of the severely shocked casualty.

The Korean war demonstrated the value of the helicopter as an adjunct to the hand carriage and ambulance transport of casualties. It was particularly useful in the forward pick-up and

evacuation of serious cases because of the difficult terrain and lack of roads. Serious cases were transported quickly and smoothly to forward surgical units or to special centres for neurosurgery, hæmorrhagic fever, or renal shut-down. Careful triage of casualties was required in order not to abuse the restricted helicopter service. An available helicopter service is a most desirable bonus to other means of transport of casualties. Unfortunately, there are many restrictions on their use. In addition, the cost is high, maintenance times are long and the load capacity is small.

The Korean conflict may have been a localized war but it was a dirty, difficult one. It served as a training and testing ground and, as in the case of all wars, medical knowledge was advanced. We feel proud of the part played by the Royal Canadian Army Medical Corps.

VITAMIN K_1 IN THE CONTROL OF PHENYLINDANEDIONE-INDUCED ANTICOAGULANT THERAPY*

A. ENGLISH, M.D.,†
S. R. TOWNSEND, M.D. and
DOUGLAS G. CAMERON, M.D.,
Montreal

IT SEEMED INTERESTING to study the effects of very small intravenously administered doses of vitamin K_1,‡ to determine whether such doses are effective in correcting excessive phenylindanedione-induced hypoprothrombinæmia, and to observe the degree and duration of subsequent refractoriness to further treatment with this drug.

Reduction of prothrombin activity is widely practised to prevent and treat thrombo-embolic disorders. Certain coumarin and 1:3-indanedione derivatives are useful for this purpose. Maintaining the prothrombin concentration in the range 30 to 10% of normal is effective and safe, but below this range hæmorrhage may occur. Fortunately, vitamin K_1 rapidly corrects the prothrombin deficiency induced by these groups of drugs.[1 to 5] Fifty to 100 mgm. of vitamin K_1 administered intravenously will usually control hæmorrhage.[6, 7] Following single doses of this magnitude, prothrombin times revert to normal within eight to 14 hours. Larger doses seldom increase the speed of this response.[6, 7] In contrast to the highly predictable effect of vitamin K_1, synthetic water soluble vitamin K preparations are unreliable. They are virtually without effect in correcting phenylindanedione-induced hypothrombinæmia.[4, 11, 12]

Considerable attention has been given to the management of hæmorrhage because it is such a serious and dramatic complication of oral anticoagulant treatment. In fact, hæmorrhage occurs in only 5% or less of patients treated in this way.[10] On the other hand, depression of prothrombin activity below the therapeutic range without actual hæmorrhage is frequently encountered. In this situation, rapid restoration of prothrombin activity to the safe therapeutic range is desirable. Large intravenous doses of vitamin K_1 will quickly obviate the risk of hæmorrhage. Unfortunately these large doses of the vitamin will restore prothrombin activity to normal, not to the therapeutic range. Moreover, patients treated in this way may be refractory to further oral anticoagulant therapy for many days.[4, 6] In these circumstances the risk of hæmorrhage is replaced by the danger of further thrombo-embolic accidents.

CLINICAL MATERIAL AND METHODS

During the past eight months, 150 patients suffering from thrombo-embolic disease were treated with phenylindanedione in this hospital. During the course of treatment, dangerously low prothrombin concentrations (less than 5%) were demonstrated in 11 patients, with whom the present study is concerned. Four of them served as controls (Group I). Four (Group II) were given single intravenous doses of vitamin K_1 emulsion calculated on a weight basis (0.1 mgm. per kilo – 6 to 9 mgm.). The other three were given single, 5 mgm., intravenous doses of this agent irrespective of weight (Group III).

After each patient came under observation, prothrombin time determinations were repeated

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*From the McGill University Clinic of the Montreal General Hospital. This work was supported by a grant from the Faculty of Medicine, McGill University.
†Research Fellow in Hæmatology.
‡Vitamin K_1 (Mephyton®) was generously supplied by Dr. J. H. Laurie of Merck & Co. Limited, Montreal.

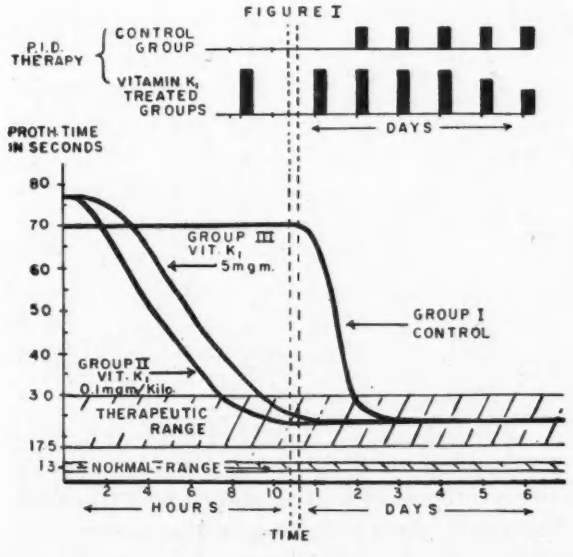
hourly for nine to 12 hours, then two to four times daily. For these determinations Quick's one-stage technique was used.[9] Tricalcium phosphate treated normal plasma was used as a diluent for normal plasma to establish prothrombin concentrations, yielding the following results:

Prothrombin concentration	*Prothrombin time*
100%	13.0 ± 1.0 sec.
30%	19.0 ± 1.6 sec.
10%	27.5 ± 2.5 sec.
5%	47.0 ± 3.0 sec.
1%	150.0 ± 10.0 sec.

RESULTS

In the four controls, prothrombin activity remained at 5% or less for 24 hours, following which it gradually returned to the therapeutic range. In the second group, prothrombin concentrations began to increase within two hours and a safe therapeutic level was reached within eight hours. In Group III, prothrombin activity was increasing within three hours and a safe therapeutic range was achieved within ten hours.

FIGURE I



When prothrombin concentrations reached the therapeutic level, prothrombin activity was maintained in this range with further doses of phenylindanedione. In the control group an amount equal to, or less than, the previous average daily dose was required. In the vitamin K_1 treated groups, resistance to further phenylindanedione therapy was slight. When prothrombin activity first reached therapeutic range, the administration of approximately twice the previous average daily dose of phenylindanedione prevented a further rapid rise in prothrombin concentration. In general, two to two and a half times the previous daily maintenance dose of phenylindanedione was required for two to five days to achieve this result. Thereafter this increased requirement diminished rapidly.

The results are shown graphically in Fig. 1.

SUMMARY AND CONCLUSIONS

This study demonstrates that very small intravenous doses of vitamin K_1 will effectively and quickly restore prothrombin activity in patients whose prothrombin concentrations have been dangerously reduced by phenylindanedione. This confirms the observations of other investigators.[6, 7, 8] Moreover, once a safe therapeutic level has been reached it is possible to maintain this by increasing the doses of phenylindanedione for a few days. Resistance to further anticoagulant therapy is slight and of short duration.

By restoring prothrombin activity to the therapeutic range rather than to completely normal levels, the danger of hæmorrhage can be averted without exposing patients to the risk of further thrombo-embolic accidents.

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TREATMENT OF HYPERTENSION

There is at the present time much anxiety among both consultants and practitioners, a feeling that they should perhaps be more active in the treatment of their many patients with raised blood pressure. I am afraid that my conclusions will be that all these [active] methods are, so far as we know, best reserved for the severer grades of raised blood pressure, and that we have no new treatment to offer to patients with mild benign hypertension.—M. L. Rosenheim, *Brit. M. J.*, 2: 1187, 1954.

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THE SURGICAL PATHOLOGY OF THE NASOPHARYNX*

P. E. IRELAND, M.D., F.R.C.S.[C],
Toronto

THIS PAPER IS PRESENTED in the hope of correlating specific pathological lesions in this area with the associated clinical symptoms. I am very much an amateur pathologist and do not propose in this short period to cover the subject completely, or to discuss all the various treatments. To quote our most revered Canadian clinician, Sir William Osler, "As is our pathology, so is our practice."

The patient with a pathological lesion in the nasopharynx may present himself with the following symptoms: (1) Obstruction to nasal breathing. (2) Postnasal discharge—purulent, mucoid or bloodstained. (3) Unilateral or bilateral deafness. (4) Involvement of various cranial nerves. (5) Unexplained firm mass in the cervical lymph nodes.

1. *Obstruction to nasal breathing.*—If there is no anterior obstruction to nasal breathing one looks for some lesion in the nasopharynx that may be causing this symptom. This may be due to a number of causes: (a) *Nasopharyngeal (naso-antral) polyp.*—Pathologically this does not differ from any other polyp with a pseudostratified columnar epithelial surface and a myxomatous type of stroma. It usually has its origin in the antrum and is of the "dumb-bell" type of polyp presenting in the nasopharynx. Some of the glands may become cystic and there will appear a large cystic area. The polyp must be removed and preferably the original area in the antrum should also be exenterated to prevent recurrence. (b) *Hypertrophy of posterior turbinate tips.*—This is usually accompanied by vasomotor and hypertrophic changes of the remainder of the nose but the change may be present in this area alone. (c) *Imperforate choana.*—Congenital absence of the usual opening in the nasal cavity from the pharynx may occur. (d) *Tumour mass.*—This may be a simple adenoid mass of sufficient size to block the posterior choanal opening of the nose. The benign juvenile fibroma of adolescent years might be present or the mass might also be a malignant tumour, which will be discussed later.

2. *Postnasal discharge – purulent, mucoid or bloodstained.*—These symptoms are largely associated with disease within the nasal cavity and sinuses, but may be the result of local nasopharyngeal pathology. Purulent discharge from the nasopharynx usually means that there is an infectious process in the antrum, posterior ethmoid or sphenoid sinuses. Mucoid discharge means an irritative lesion of the mucosa of the nose or nasopharynx. This may be due to the irritation of tobacco, dry atmosphere or other irritants; histologically, there is marked increase in the number of goblet cells in the mucosa with their increased ability to secrete mucus. Very occasionally such discharge means the presence of an isolated area of mucus retention in the vault of the nasopharynx which is then known as Tornwaldt's bursa or cyst. In this area of blocked crypts, the mucoid secretion is retained and squeezed out at intervals in large amounts.

When there is a history of bloodstained discharge from the nasopharynx one can only think of a local, ulcerative lesion in this area, or in the nose or accessory sinuses. This means that either a severe inflammation or a tumour is present; the latter is more likely. Bleeding implies the erosion of a vessel and the pathological process which is necessary to this factor.

3. *Unilateral or bilateral deafness.*—The absence of patency of the Eustachian tube is a factor in the development of middle ear deafness. Any obstruction on the lateral wall of the nasopharynx will interfere with this function. Perhaps the most common cause of this interference is the obstruction due to lymphoid tissue, either as a mass overhanging the orifice, or within the tubal orifice. Any tumour mass which encroaches on the opening of the tube, whether a benign nasoantral polyp or a malignant tumour, has the same effect.

4. *Involvement of various cranial nerves.*—In any case of tumour involving the cranial nerves of the supratentorial area one should think of a pathological process arising in the nasopharynx. Tumours in this area do tend to promote bone destruction in the vault of the nasopharynx and also to extend through all the existing foramina in the base of the skull. Many bizarre neurological findings can be explained by careful examination of the nasopharynx accompanied by roentgenological investigation of the base of the skull for destruction of bone.

5. *Unexplained firm mass in the cervical lymph nodes.*—Too often one finds that the first symp-

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†From the University of Toronto, Department of Otolaryngology.

tom of a malignant tumour in the nasopharynx is a firm fixed mass in the cervical lymph nodes. The primary tumour in the nasopharynx may be small enough to be symptomless or unnoticed on routine examination. It may occur in the vault or in the "fossa of Rosenmüller," behind the Eustachian cushion. This tumour is often a highly malignant type of transitional-cell carcinoma, or lympho-epithelioma. Basal-cell carcinoma and lymphosarcoma occur much less frequently and melanotic sarcoma rarely.

NASOPHARYNGEAL (NASO-ANTRAL) POLYP

This is really not a true tumour of the nasopharynx but the extension of a simple antral polyp, first to the nasal cavity and then to the nasopharynx through the choana. It is probably inflammatory in origin. The *gross* appearance is of a tense, pearshaped mass presenting in the nasopharynx. The narrowed constriction of the stalk passes through the ostium of the antrum. The dependent portion in the nasopharynx may be composed entirely of a large cystic dilatation.

The *microscopic* appearance is of a loose, œdematous reticulum with a moderate small cell infiltration and a few polymorphonuclear leucocytes and eosinophils. The epithelium is of a ciliated, stratified columnar type. As mentioned in the paragraph above, large cystic spaces may be found, lined with low columnar epithelium and filled with mucoid material.

The *treatment* of these cases is usually easy. A snare can be passed to the nasopharynx and threaded over the mass with a finger through the mouth. A large amount of fluid may escape when the tumour is avulsed if there is a cystic degeneration. The patient must be warned that a recurrence is possible and a Caldwell-Luc operation may occasionally be necessary to remove the other half of the "dumb-bell."

IMPERFORATE CHOANA (CHOANA OCCLUSION)

This is a cause of marked nasal obstruction due to the persistence of the bucconasal membrane in development. It is more common in females and may be unilateral or bilateral. It may be complete, or a small opening may persist. The pathological picture is largely of a bony, occluding mass with a central area of membrane composed of fibrous tissue with an epithelial layer on each surface.

The treatment consists of the use of a long sphenoid punch which can be forced through the membranous portion of the obstruction and the bone and fibrous tissue widely removed. A dental composition or plastic prosthesis must be put in place and kept for at least 12 weeks to prevent recurrence of the closure.

NASOPHARYNGEAL ADENOIDS

Obstruction to nasal breathing due to lesions in the nasopharynx is most commonly due to the hypertrophy of masses of adenoid tissue in this area. There must be included in this consideration that portion of Waldeyer's lymphatic ring found in the vault as well as that on the lateral walls in the region of the Eustachian tube. Similar active lymphoid tissue has also been demonstrated within the entrance of the tube. The etiology of this hyperplasia is not known. In a very few cases it is found soon after birth, but most commonly occurs between the ages of three and 12 with a regression after puberty and complete involution at 18 years of age. It may be found, however, at any age, even over 50. It affects both sexes equally and the rich and well-nourished as well as the poor. It may be associated with other areas of lymphoid hypertrophy such as the thymus gland.

Adenoids may appear in three main forms: (a) a diffuse friable mass of lymphoid tissue scattered over the whole wall and vault of the area; (b) a central heaped-up cushion in the vault with varying amounts of peripheral islands; (c) an established adenoid tonsil structure. There is a smooth soft cushion with longitudinal ridges and deep furrowed crypts. It is wider and thicker at its upper attachment in the vault and becomes thin and narrow as it approaches the level of the soft palate.

The *microscopic* picture is that of groups of mature lymphocytes in a small amount of reticulum. Germinal centres may be present but are much less frequent than in the pharyngeal tonsil. The surface is covered with stratified squamous epithelium at the inferior border, which gradually shows a transition to the pseudo-stratified columnar epithelium of the vault. The area of transition has been given the name of transitional epithelium and consists of a low cuboidal type of cell with dark staining nucleus and cytoplasm.

The *treatment* of adenoid tissue is removal. It is difficult to be certain of complete removal by any known method. I think that careful retraction of the palate and "peeling off" the tissue

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from the deep structures by means of a broad punch is the safest method. A curette may be used later, but even the most careful operation may leave islands that will later hypertrophy. I would like to make an honest plea for the judicious use of radium applicators. I believe that they are dangerous and have been used far too much. They should be reserved for very occasional cases and are not without very grave hazards. I would like them to be used in a few centres and certainly not on adult patients. I think the intractable cases may be better treated by the cobalt bomb.

TORNWALDT'S CYST (TORNWALDT'S DISEASE)

In 1885 Tornwaldt described an infection of the bursa of the nasopharynx which might produce an enlargement of the area behind and above the adenoid mass. This might rupture and produce a fistulous track from this bursa, giving immediate and recurring discharge. It is generally accepted that such a condition may be found, but that it is not in the pharyngeal bursa, but more likely is due to an obstruction and coalescence of the deep adenoid crypts with the continuing of the exfoliation of their epithelial lining. This is not unlike the process found in the epithelial inclusion in blocked sweat glands or in cholesteatoma. Infection in this area results in the formation of putty-like, foul smelling, caseous material which may be expressed from time to time by the pressure created. Microscopically this material is very similar to that of infected cholesteatoma with masses of degenerated keratin tissue, polymorphonuclear leucocytes and the occasional collection of cholesterol crystals.

The treatment of these cases is removal when one can feel assured that the large cheesy masses of foul material come from the nasopharynx. If there is a spongy area in this location, removal is essential. This can best be done under a general anæsthetic with an adenotome. If we are to concede that the condition is due to retention in crypts of this area, this is all that is necessary. However, one should carefully retract the palate and use a punch well up to the pharyngeal aponeurosis in order to be sure the whole area is uncapped.

BENIGN JUVENILE NASOFIBROMA (FIBRO-ANGIOMA, ETC.)

These tumours, in spite of the publicity given to them, are relatively rare and, according to Mosher, are one of the disappearing lesions. The most extensive series has been reported by the Mayo Clinic, with 63 cases in 40 years. These tumours have unusual features in that they are a disease of the teens and almost entirely confined to the male population. There is a marked tendency to regression in adult life.

The origin of these tumours is doubtful. It is generally accepted that they are derived from the fibrous tissue of the vault of the nasopharynx at the junction of the area of fusion between the pharyngeal aponeurosis and the buccopharyngeal fascia. Their origin is usually from the base of the sphenoid, but they may have firm attachments to the pterygoid plate, the septum or even to the cervical vertebræ. They may vary in size from the proportion of a walnut to that of a fist, with wide local invasion. The tumour is locally expansile from the point of origin but does not produce secondaries in regional lymph nodes. The *gross* appearance is of a firm, irregular, reddish, tumour mass with many blood vessels on its surface. It is of a hard rubbery consistency.

The *microscopic* appearance is of adult connective tissue cells with no distinct capsule condensation. The blood vessels usually are of two types: (a) normal vessels with all walls similar to a normal blood vessel; (b) areas of blood spaces lined with a single layer of endothelial cells showing evidence of proliferation. The proportion of these latter thin-walled, hyperplastic blood spaces to the amount of fibrous tissue present is usually important. It is used in deciding whether the tumour is designated a fibroma, fibroangioma or, occasionally, angiofibroma. The absence of contractile tissue and the thin walls of the large spaces are important factors in the hæmorrhage which occurs, either spontaneously or at operative procedures. Many collections of round cells within the fibrous tissue fibres have probably accounted for the occasional diagnosis of embryonal sarcoma, which is incorrect.

The treatment of nasopharyngeal fibroma is as follows: (1) *Palliative.*—If these tumours are not large and are seen late in the teens, one might watch them and they may regress. They are occasionally found accidentally and are quite symptomless. (2) *Irradiation versus surgical removal.*—At one time the Mayo Clinic surgeons, who have the largest series of cases, stated that all should have irradiation and no surgery. They have changed from this and now advocate irradiation plus surgery. It is essential, before any

surgical procedure, to destroy the actively growing blood spaces before proceeding to surgical removal. This can be done by high voltage therapy, implantation of radon seeds or the use of the cobalt bomb. Operation may be done by splitting the palate for better exposure, or by the direct approach of the Denker operation. I was pleased to find that Dr. Figi agreed with me at the American College of Surgeons that perhaps the Denker approach was best. Diathermy is essential in complete eradication. Occasionally a second operation must be performed.

MALIGNANT TUMOURS OF THE MOUTH, PHARYNX AND NASOPHARYNX

Eggston has quoted Ewing as saying that anyone thoroughly acquainted with the malignant tumours of this area would have an extensive knowledge of tumour pathology. There is a wide variance of opinion about some of these lesions and in this paper the author is attempting only to present a reasonable basis for consideration of their clinical significance from the point of view of relative risk to the patient. A discussion of sensitivity to radiation treatment will be included.

THE PHARYNX AND NASOPHARYNX

Malignant tumours in this area closely resemble those of the tongue in that they differ in structure, degree of malignancy and radiosensitivity depending on their location. The usual tendency is for those behind the tonsil to present more anaplastic tendencies, although there is an overlap in this region. Most of these tumours must be classified as epidermoid carcinoma, but there is a further division into two distinct subgroups: (a) transitional cell carcinoma; (b) lympho-epithelioma. Both the transitional cell carcinoma and the lympho-epithelioma present important differences from a squamous cell carcinoma, which is the characteristic tumour of skin and many parts of the mouth and upper food and air passages. They do not form a squamous type of epithelioma with cell nests and cornification.

The division of these two types of tumours runs the gamut of disagreement by the various pathologists and it has been suggested that both types might be classified as anaplastic malignant tumours or, if one wishes to use the Broders classification, as type four tumours. Clinically this would seem advisable and they will be discussed as such first, an attempt being made later to separate them by their microscopic appearances. The cellular content is that of round or polyhedral cells with a large, hyperchromatic nucleus, occupying most of the cell. The cells vary in size and present many mitotic figures.

The primary lesion may be small, undetected and difficult to find. Clinical evidence of secondaries in the neck may lead to a most thorough search; in occasional cases, the lesion is found only on biopsy by adenoid curette. Palpation of the tonsil, pharynx, and nasopharynx is most important as the tumour may spread by deep infiltration. For some unknown reason it is a frequent finding in Chinese patients.

Although primary lesions are difficult to detect, early involvement of cervical lymph nodes is very striking. In the absence of a primary tumour on examination, lymphosarcoma may be diagnosed in error, but lymph node biopsy will demonstrate the true cell type. In marked contrast to squamous cell epithelioma, metastases to the lung, liver, and bones are very common.

The radiosensitivity of these tumours is very striking and they seem to melt away on treatment. This is often not permanent arrest, but regression of the tumour, which will soon recur.

One might summarize the consideration of these two types of tumour by saying that they are probably a group of highly anaplastic epidermoid carcinomas. They are characterized by the tendency to inconspicuous primary lesions but massive involvement of the regional lymph nodes and distant areas of visceral metastases. Because of their anaplastic nature they are very radiosensitive and could be confused clinically with the sarcoma group. Biopsy should prevent any such mistake.

CONCLUSIONS

This has been an attempt to correlate the pathological findings in diseases of the nasopharynx with the clinical picture. Too often this is a hidden area of diseases which may end fatally. Many patients complain of symptoms relative to this area which are usually of little importance, but on occasion may be of grave significance.

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Banting Institute, 100 College St.

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THE COMMON OCCURRENCE OF ENDOMETRIOSIS IN YOUNG WOMEN

M. BRUSER, M.D.,* *Winnipeg, Man.*

ENDOMETRIOSIS is a fascinating disease which (1) resembles the congenital lesion of ectopic tissue but is not congenital; (2) resembles malignancy in the manner of its spread but is not malignant; (3) resembles an inflammatory condition by virtue of the reaction it produces in surrounding tissue. It is even doubtful whether it ought to be classified as neoplastic, Kottmeier (1952) putting it in a separate classification of its own; Novak (1947) includes it under the heading of "non-neoplastic cysts of the ovary," and Greenhill (1954) puts it under "benign tumours and endometriosis." Further, it is the opinion of some gynæcologists that trauma to the pelvic peritoneum, e.g. surgery, may, in susceptible women, cause the development of endometriosis where it did not exist before.

So here is a distinct clinical and pathological entity which is not a congenital condition, but resembles one; is not a malignant condition, but in some ways resembles one; is not of traumatic origin, but sometimes may be; and is not clearly neoplastic. Is there any other such disease? Clinically, too, it can be very puzzling, and one of the reasons for this difficulty is the popular misconception concerning the age incidence. For instance it is not commonly recognized that sometimes a case which clinically is highly suggestive of ectopic pregnancy turns out to be a leaking endometrial cyst; under other conditions the innocent appendix is removed, with no relief of symptoms. Often the diagnosis could have been made, had it been realized that endometriosis can occur in young women. It is this aspect of the disease that is discussed in this paper.

It is interesting to follow the references to the age incidence of endometriosis through some of the older textbooks to the more modern ones, and then to the latest literature. The disease was first identified and well described in 1893 by von Recklinghausen. Eden and Lockyer (1917) give a superb review of the literature to that date, and in discussing a series of 20 cases reported from Germany in 1908 note that all were in women aged from 32 to 51, average 41. In another series of 66 cases reported in 1905 nine were under 30; one patient had been reported who was 25 years of age.

Blair Bell (1934), who introduced the term endometriosis in 1922, said that "signs and symptoms are seldom made manifest before the age of 30 years; often advice is not sought for some years later." Novak (1947) states that "endometriosis is a disease of reproductive life, occurring most frequently between 30 and 40 years of age." Wilfred Shaw (1948) says "The maximum age incidence is between 30 and 40." He makes no mention of its possible occurrence in younger women. Browne (1950) begins to make definite references: "The age incidence of genital endometriosis is usually from 30 to 50 years though it may occur in much younger women. In the cases of Kelly and Schlademan the youngest was aged 20 and the oldest was 65." McLeod (1950) says "Endometriosis is only found in patients during the period of active sexual life, but is particularly prone to occur between the ages of 30 and 50 years . . . it is possible that endometriosis is responsible for many cases of prolonged dysmenorrhœa and obscure pelvic pain in young girls."

In view of this powerful body of experience and opinion, often dogmatically stated, it is inevitable that the teaching regarding the age incidence has always repeated that phrase "age 30 to 40." The fact that the disease can occur in much younger women has been muted, and by many of us forgotten. Fallon (1946) was one of the first to stress its occurrence in young women, and he did it from three points of view: (1) it is a sterilizing disease, and hence should be treated in youth; (2) it tends to occur after about five years of menstruation without pregnancy; and (3) whenever abdominal surgery is required in young women the pelvis should be explored. In his series of 225 cases of proven endometriosis, 4% were in women under 20, and one was in a girl of 13. If one includes cases which at operation were clinically unmistakable but microscopically unproven, the incidence under 20 would be doubled to 8%. The figures reported by Siegler and Bisaccio (1951) are very similar: "Of 67 operatively proved endometriosis cases, 8.9% were under 25, and a further 15% were under 30 years of age." In other words, 24% were under 30. This is quite different from the older teaching which stressed that phrase "30 to 40" so repeatedly. Almost one-quarter of these cases occurred under the age of thirty. Counsellor and Crenshaw (1951) reported that of 1,342 women with endometriosis operated upon at the Mayo Clinic 4% were under 25. A further 4,000 cases (approximately) were diagnosed as endometriosis but not subjected to operation, and of these the large majority were under 30. They state: "Should more of these patients be treated surgically, there would be a marked increase in the incidence between 20 and 30 years." One more paper may be mentioned at this point. Pratt *et al.* (1952) described 10 cases of ruptured chocolate cysts, and of

*Mall Medical Group, Winnipeg; Assistant Obstetrician and Gynæcologist, Misericordia Hospital, Winnipeg.

these, five were women in their twenties. From these reports, and from others in the recent literature, it is becoming more evident that endometriosis can and commonly does occur in women under the age of 25.

SYMPTOMS

This paper presents a series of 15 cases of endometriosis in women who were 25 or under at the time their first symptoms appeared. These patients were seen in private practice over a period of five years. No patient was operated upon unless symptoms were severe; and only after a full discussion with the patient and usually also with her husband. Table I summarizes the preoperative symptoms, and Table II their relative frequency. Tables III and IV show the ages of onset and at diagnosis, any previous operations, and the obstetric history of the patients.

Obviously this is too small a series from which to draw unqualified conclusions. Nevertheless, certain interesting items emerge. It will be noted that all suffered from pain of one sort or another. Remembering that signs and symptoms bear little or no relation to the extent of the disease it is evident that quite often in these younger women it is pain which demands relief, even in the absence of definite signs of endometriosis preoperatively; and this explains why such a large percentage had pain of one type or another, even in the presence of small lesions. For example, all had lower abdominal pain, compared to only 40% in the series of Siegler and Bisaccio, only about half of whose cases required surgery.

TABLE I.

SYMPTOMS (PREOPERATIVE)

Case No.	*Dysmenorrhœa*	*Menorrhagia*	*Metrorrhagia*	*Abdominal pain*	*Backache*	*Dyspareunia*
1	No	Sometimes	Yes	Yes	No	Always
2	Yes	Yes	Yes	Yes	Yes	Yes
3	Yes since age 20	Yes since age 20	Yes since age 20	Sometimes since 18	Yes since 18	No
4	Yes	Yes	Yes	Yes	Yes	Yes
5	Yes	No	Yes	Yes Also pain with bowel movements	Yes	Yes
6	No	Yes	Sometimes	Sometimes	Yes	Severe
7	Yes	No	Yes	Sometimes	Yes	Yes
8	No	Yes	Yes	Yes	Yes	Yes
9	Yes	Yes	Yes	Yes	No	Single
10	Yes	Sometimes	Sometimes	Yes	Yes	Yes
11	Yes	No	No	Yes	Yes	Single
12	Yes	Sometimes	Sometimes	Yes	Yes	No
*13	Yes	Sometimes	Sometimes	Yes	Yes	No
*14	Yes	No	No	Yes	No	Single
*15	Yes	No	Yes	Yes	Yes	Sometimes

*Cases 13, 14 and 15 were not operated on.

TABLE II.

INCIDENCE OF SYMPTOMS

	Siegler and Bisaccio (1951) %	*Present series*	
		All cases %	*Microscopically confirmed* %
Dysmenorrhœa	76	82	66
Menorrhagia	51	70	78
Metrorrhagia	43	88	100
Low abdominal pain	42	100	100
Backache	37	82	78
Dyspareunia	24	*54	78

*Three cases (20%), including one of the histologically confirmed ones, were in virgins.

Note that: (1) The average age at the onset of symptoms was under 20 in over half of these cases. (2) Four patients had had appendectomy, and this operation was advised in one other case. It may have been endometriosis which caused these symptoms. (3) Of the entire 15 patients, seven have had no children; and of these, one is still single. One who was single at the time of diagnosis has subsequently married and had a child. (4) It cannot be demonstrated statistically, but the impression was that many of these girls were of a "neurotic" temperament. It is mere guesswork whether this is an accidental association or whether a connection exists; for example, is there a state of nervous tension engendered by repeated or constant pain, or apprehension concerning the next menstruation, or the next act of coitus, or the cumulative emotional effect of failure as a wife, both on account of pain and possibly infertility?

TABLE III.

	Microscopically Confirmed Cases								
Case No.	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
Age at onset.....	24	11	18	21	25	20	about 18	24	about 20
Age at diagnosis....	24	21	20	25	31	22	25	25	30
Previous operations.	0	0	*0	2	1 appendectomy	0	1 appendectomy	0	1 D & C
Children.....	0	single	0	0	2 before op.	2 since op.	0	2 before op.	0

*Appendectomy advised at 18.

TABLE IV.

	Cases not Microscopically Confirmed					
	Operated on			*Not operated on*		
Case No.	*10*	*11*	*12*	*13*	*14*	*15*
Age at onset.....	22	15	17	22	18	18
Age at diagnosis.....	24	19	22	28	20	19
Previous operations.....	See history	Appendectomy age 16	Appendectomy age 18	0	0	0
Children.....	0	*1 since op.	2 since op.	0	single	2

*Was single at time of operation, subsequently married.

Physical Signs

Tender, firm nodules in the pouch of Douglas, on the uterosacral ligaments, on the back of the uterus at about the level of the internal os; these are almost pathognomonic in a case where previous infection can be ruled out. Palpably enlarged, tender, fixed ovaries are sometimes found; and the uterus in fixed third-degree retroversion with hard, tender nodules on the back of it is again almost certainly diagnostic.

Treatment

Bacon (1949), in a report on 138 cases, found that the results were in no way correlated with the nature or extent of the lesion. He shows that 30 to 40% were treated conservatively with no relief, requiring later more radical surgery, or in some cases irradiation. This report and many others, including that of Siegler and Bisaccio (1951), stress once more the insufficiently appreciated fact that there seems to be no relationship between the nature and location of the disease and the severity of the symptoms, or the degree of relief obtained by conservative surgery. Counsellor and Crenshaw (1951) were not in favour of surgery in younger patients, and operated on only about 25% of them. Their impression was that most of these girls could be carried along by medical methods until older, with probably the same results as are achieved by conservative surgery. In commenting on this paper, Te Linde said that he disagreed on this point, and gave the following figures in support: of 64 such patients operated upon, 26 had 38 pregnancies. He argues that it is often better to operate early, while conservatism is still possible. Novak, at the same meeting, pointed out that there are many women, even young ones, with palpable nodules, or residual palpable areas of endometriosis after conservative operation, who have few or no symptoms, and these women should not be operated upon again on the basis of these findings. Of the series reported by Schmitz and Towne (1948), about 48% of cases treated conservatively (i.e. with retention of the uterus and at least part of one ovary) required secondary surgery or radiotherapy, and they believe this is justifiable because in the interim over one-quarter of these women bore children. In his comment on this paper, Randall states that in the series at Buffalo General Hospital 94% of cases under 35 were treated by conservative operation and in 80% of these women the childbearing function was preserved.

In the present series, 12 cases were subjected to operation; in nine of these the diagnosis was microscopically confirmed.* Goodall (1943) states

*Presence of endometrial glands and stroma.

that in only one-third of cases where clinically and grossly there is undoubtedly endometriosis will the pathologist find definite endometriosis.

SUMMARY OF CASE HISTORIES

1. Onset at age 24. Menometrorrhagia, abdominal pain, dyspareunia. Operation at age 24—resection of affected areas. Still has her symptoms, although to a much lesser degree. Her psyche plays a large part. No pregnancies.

2. Onset at age 11. Dysmenorrhœa, menometrorrhagia, abdominal pain, backache, dyspareunia. Operation at age 24—resection, presacral sympathectomy, ovarian sympathectomy and suspension. Pain was relieved, but a second operation was required two years later because of a 3″ cystoma simplex, and at this operation there was no apparent endometriosis in the pelvis. Within the past few months there has been a gradual recurrence of pain, and she still has bouts of menometrorrhagia. Single.

3. Onset at age 18. Dysmenorrhœa, menometrorrhagia, abdominal pain, backache. No dyspareunia. Operation at age 20 was for suspect appendicitis—resection of areas of endometriosis. Relief of all symptoms except mildly excessive menstrual flow at intervals. No pregnancies.

4. Onset at age 21. Dysmenorrhœa, menometrorrhagia, abdominal pain, backache, dyspareunia. Three operations: (1) age 25, resection; (2) age 27, left oophorectomy; (3) age 28, resection and right oophorectomy. Relieved of all symptoms. Gives herself a "period" (œstrogen withdrawal bleeding) from time to time for the psychological effect, and these are painless. The intermittent use of œstrogens also probably helps in the maintenance of normal healthy vaginal mucosa.

5. Onset at age 25. Dysmenorrhœa, metrorrhagia, abdominal pain, backache, dyspareunia, and pain with bowel movements. Appendectomy at age 15, no relief. Operation at age 31—resection, presacral sympathectomy, suspension. Occasional dysmenorrhœa and dyspareunia, not severe. Periods normal. No backache or abdominal pain. No pain with bowel movements. Two children before operation.

6. Onset at age 20. Menorrhagia, backache, severe dyspareunia. No dysmenorrhœa. Occasional metrorrhagia, and abdominal pain sometimes. Operation at age 22—resection and suspension. Complete relief of all symptoms. Two children since operation.

7. Onset at about 18. Dysmenorrhœa, metrorrhagia, backache, dyspareunia. Attacks of abdominal pain. No menorrhagia. Appendectomy at age 18, no relief. Dilatation and curettage twice with no relief. Operation at age 25—resection of bilateral chocolate cysts, and diffuse endometriosis with dense adhesions. Complete relief of all symptoms except for episodes of rectal pain and diarrhœa, which have no relation to menstrual cycle. Has hæmorrhoids and this may be the source of her pain. On vaginal examination the pelvis feels much the same as preoperatively. No children.

8. Onset at age 24. Menorrhagia, metrorrhagia, abdominal pain, backache, dyspareunia. No dysmenorrhœa. Operation at age 25 and 26. First operation October 1953—resection and suspension. There was no relief at all, and a second operation was necessitated by severe pain four months later. This operation consisted of subtotal hysterectomy with affected ovaries. It is too early at the time of writing to assess the result. Two children before operation.

9. Onset at about 20. Dysmenorrhœa, menometrorrhagia, abdominal pain, backache. Single. Dilatation and curettage at age 22 with no relief. Resection of affected areas and suspension at age 30. Menorrhagia and pain continued postoperatively, and became continuously worse. Given sterilization dose of x-ray therapy seven years later with complete relief of all symptoms.

10. Onset at age 22. Dysmenorrhœa, menometrorrhagia, abdominal pain, backache, dyspareunia. Operation at age 24 (1949)—resection of typical areas of endometriosis on left uterosacral ligament, back of uterus, and on peritoneum of uterovesical pouch on left side. Spontaneous complete abortion at ten weeks, 1951. Recurrence of all symptoms after that, progressively worse, and second operation in March 1953: intense pelvic adhesions and no microscopic evidence of endometriosis. Well until November 1953; symptoms all recurred, and at third operation in March 1954 total hysterectomy and bilateral oophorectomy was performed. It is too early at the time of writing to assess the result. No children.

11. Onset at age 15. Dysmenorrhœa, abdominal pain, backache. Single. Appendectomy at age 16 with no relief. Operation at age 19—clinically definite endometriosis areas throughout the pelvis. All resected, and presacral sympathectomy. A large degree of overlay of the psyche in this case makes assessment difficult. She appears to be well and has no pain. She says she has heavy and prolonged periods, with spotting before and after. Has been married and had one baby since her operation. Secondary infertility under treatment now.

12. Onset at about age 17. Dysmenorrhœa, abdominal pain, backache. No dyspareunia. Occasional menorrhagia and metrorrhagia. Appendectomy at age 18 with no improvement. Resection and suspension at age 23. Some relief of pain. No menstrual irregularities. Two children since her operation.

13. Onset at age 22. Diagnosis at age 28. Dysmenorrhœa, abdominal pain, backache. Occasional menometrorrhagia. No dyspareunia. Has nodules on both uterosacral ligaments, all through the pouch of Douglas, and on the back of the uterus. No operations. No pregnancies—uses contraception.

14. Onset at age 18. Diagnosis at age 19. Dysmenorrhœa, abdominal pain. No menstrual disturbance. Single. Pelvic findings typical. Not seen since she was informed that an operation was not indicated by her relatively minor symptoms.

15. Onset at age 18. Diagnosis at age 22. Appendectomy at 18 with no relief. Dysmenorrhœa, metrorrhagia, abdominal pain, backache, dyspareunia. Typical pelvic findings. Has had two children since the diagnosis was made and is asymptomatic at the present time.

It may be noted that of the conservative operations, three were complete failures, two patients requiring two further operations resulting in sterilizations, and the other patient one. One patient required radiotherapy seven years after her conservative operation, with complete relief of all symptoms. The remaining cases have been either completely or satisfactorily relieved of their symptoms.

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CONCLUSIONS

1. Endometriosis occurs in young women sufficiently often to demand serious consideration in the differential diagnosis of conditions causing lower abdominal pain, dysmenorrhœa, dyspareunia, backache, menorrhagia, or metrorrhagia; and especially if several of these symptoms are combined.

2. A presumptive diagnosis may be made on the basis of symptoms and signs; the more typical these are, the more definite one can be. It must be borne in mind that even after operation the diagnosis may not be absolutely assured, although with typical pelvic findings one need not too slavishly accept a negative pathology report as final.

3. Difficult as this condition is to diagnose, it is even more difficult to treat in these younger patients. Treatment seems to depend on the following factors: (a) age; (b) parity; (c) severity of the symptoms, and rarely on the size of the lesions; (d) capacity of the patient to understand her condition, and her ability to live with it. This is sometimes the deciding factor. For example, a girl aged 25 with three children and a low pain threshold, who is totally incapacitated for a week or more out of every month and who is unable to co-operate with her husband sexually, is entitled to have a major procedure performed. On the other hand, a girl with no children and minimal symptoms can usually be encouraged to accept her condition and carry on with it. It is the cases between these extremes which can be extremely difficult, and each case must be judged on its merits. It is unpleasant to be forced to remove both ovaries in a young woman, either surgically or by means of radiotherapy; unfortunately it is sometimes advisable. It sometimes seems rather a better course than to watch the painful disintegration of a barren marriage. In some cases it is the patient herself and her husband who, after a full explanation (to the limit of their capacity to understand), must make this most important decision.

Finally one may conclude from a study of these cases that conservative surgery, although it will sometimes fail to relieve symptoms or prevent recurrence, has a definite place in the treatment of this condition, for at least temporary relief of pain and bleeding, and possibly the prevention of further advancement of the condition and of sterility.

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RÉSUMÉ

L'endométriose se présente assez fréquemment chez les jeunes femmes pour entrer en ligne de compte dans le diagnostic différentiel des causes de douleurs dans le bas-ventre, dysménorrhée, dyspareunie, maux de dos, ménorragie et métrorragie, tout particulièrement s'il existe une combinaison de plusieurs de ces symptômes. Un diagnostic présumé peut être posé d'après un certain nombre de symptômes et de signes; plus ceux-ci sont caractéristiques, plus le diagnostic peut être catégorique. On doit se rappeler que même après opération, le diagnostic peut ne pas être nécessairement établi; tout de même, en présence de lésions pelviennes typiques, il n'est pas nécessaire d'accepter sans restriction un rapport anatomo-pathologique négatif. Si difficile que puisse être le diagnostic de cet état, le traitement chez les jeunes malades l'est encore davantage. Ce traitement peut être modifié d'après (1) l'âge de la malade, plus particulièrement en fonction des années de vie sexuelle active; (2) la gravité des symptômes; (3) quelquefois, l'étendue des lésions, et enfin (4) la capacité de la malade à comprendre son état et à s'en accommoder. Cette dernière considération peut quelquefois être la raison décisive; par exemple, telle jeune femme de 25 ans, mère de 3 enfants, et possédant peu de résistance à la douleur, complètement terrassée chaque mois pendant une semaine ou plus, et incapable d'offrir à son mari aucune collaboration sexuelle, est en droit de subir une intervention radicale. D'un autre côté, une jeune fille, sans enfant, et ne présentant que des symptômes légers, doit être encouragée à supporter son état sans plus. Chaque cas doit être évalué individuellement, et il en est à mi-chemin entre ces extrêmes qui peuvent être extrémement difficiles à résoudre. Il est regrettable d'enlever les ovaires d'une jeune femme par chirurgie ou radiothérapie; malheureusement, cela s'impose dans certaines occasions, car une telle solution semble préférable à la désintégration douloureuse d'un mariage stérile. Quelquefois, on doit laisser les intéressés prendre eux-mêmes la décision après leur avoir donné toutes les explications possibles. La chirurgie conservatrice, même si elle ne peut pas toujours soulager les symptômes ou prévenir leur réapparition, occupe une place bien déterminée dans le traitement de cet état par le soulagement (ne fût-il que temporaire) de la douleur et de l'hémorragie et des chances qu'elle présente d'enrayer le progrès des lésions et d'éviter la stérilité. M.R.D.

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THE TREATMENT OF HYPOSPADIAS*

FREDERICK PILCHER, M.D., M.Sc.,
Calgary, Alta.

AN OPERATION for the correction of hypospadias must accomplish certain definite objectives in order to produce a result that will be thoroughly satisfactory to the patient. First, the deformity must be corrected. This means that the penis must be perfectly straight on erection, and a new urethra must be formed to the end of the penis in such a manner that urination can be accomplished in the standing position and that in later life insemination may be successful. At the same time, the operation itself must not produce any new complications such as stricture, fistula, or hair in the urethra. Finally, the operation should be technically simple enough for a competent surgeon to perform locally, thus sparing the patient the expense and inconvenience of being referred to a highly trained specialist or plastic surgeon. I propose to discuss the most widely used methods for correcting hypospadias, and show why the Cecil operation seems best to fulfil all these requirements.

Hypospadias results from failure of fusion of the urethral folds in the midline. There is a congenital absence of the floor of the urethra extending for a variable distance inward from the end of the penis. It is further complicated by a downward curvature of the penis which is sometimes erroneously called chordee.[14] This is alleged to be caused by a heavy fibrous band extending from the abnormal opening to the glans penis. Such a band may occasionally exist, but more often it is absent. Actually, the roof of the urethra is present but its corpus spongiosum is fibrous and contracted and adherent to the adjacent corpora cavernosa so that the skin on the under side of the penis is not freely movable on the shaft of the penis.

The surgical correction of hypospadias involves two procedures, that of correcting the downward curvature of the penis and that of forming an extension to the urethra. It has been my practice to straighten the penis at the age of two. An earlier age is suggested by some surgeons, but at the age of two the child probably can be anæsthetized more safely. The penis remains perfectly straight thereafter as the child grows and develops. The new urethra should be completed before school age in order that the boy may urinate normally in a standing position and not suffer psychological embarrassment. Should the condition have been neglected, it is still possible to obtain good results at almost any age. The oldest boy on whom I have operated was 14 when the straightening operation was performed and a good result was obtained.

Correction of the downward curvature is a well-standardized procedure. Simple dissection just beyond the abnormal opening will permit correction in many cases. It may be necessary to dissect all of the fibrous bands on the under side of the penis and the lateral sides of the corpora cavernosa as well. In some instances the fibrous bands between the corpora cavernosa must also be dissected. Occasionally it is necessary to dissect the corpus spongiosum from the corpora cavernosa and allow the hypospadias opening to drop further back before complete straightening is accomplished. To ensure that the correction is adequate it should be possible to overextend the penis.

To cover the area exposed when the curvature is corrected, there are four methods for transferring the prepuce to the under side of the penis.

1. The Duplay (Heineke-Mikulicz)[5] procedure was the first to be described and has been recently improved. Many surgeons find it satisfactory in moderate degrees of hypospadias. The penis is straightened by means of a wide lateral incision beyond the abnormal opening followed by thorough dissection of the fibrous bands between the corpora cavernosa. A longitudinal closure of the wound, preferably with silk sutures, serves to cover the denuded area.

2. In the Blair[2] operation the prepuce is completely dissected from the penis and lateral flaps are swung around on each side to cover the under surface.

3. The Nesbit[21] operation consists of dissecting the prepuce from the end of the penis and then making a longitudinal slit in the prepuce through which the penis is passed. The large

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flap of prepuce is used to cover the denuded under surface.

4. The Edmunds[15] two-stage operation is no longer used as it probably has no advantage over the Blair or Nesbit one-stage methods.

When the tissues are soft, at least six months after the penis has been straightened, an extension to the urethra may be formed from the hypospadias opening to the end of the penis. It is said that more than 150 different procedures have been employed to form a new urethra. This great number is evidence that results have not been wholly satisfactory for one reason or another. The history of the development of these procedures is well reviewed in the monograph by Cecil[7] and by other authors who appear in the bibliography of this article.

Space does not permit a detailed description of all of the operative procedures for forming a new urethra. However, I will mention here the characteristic features and shortcomings of some of the most widely used procedures and outline in considerable detail the Cecil operation, pointing out why this operation or a modification of it is most likely to produce the desired results.

Regardless of method, it is necessary first to divert the urine temporarily by means of perineal urethrostomy or suprapubic cystostomy in order to keep the operative area dry while the wound is healing.

The operative procedures for formation of the new urethra can be grouped into seven types of urethroplasty, using:

1. Subcutaneous skin strip (Duplay, Marion, Browne).
2. Penile skin alone (Thiersch-Duplay).
3. Free inlay graft of skin, veins, appendix, etc. (Nové Josserand).
4. Pouch of skin from adjacent penis and scrotum (Ombredanne).
5. Tubes of skin from adjacent scrotum and thigh (Gillies tubes).
6. Combination of penile and scrotal skin (Bucknall).
7. Skin from the under side of the penis for the urethra and scrotal skin for the cover (Cecil, Cabot, Blair, Wehrbein, and Smith and Blackfield).

1. The oldest method for forming a new urethra is that of Duplay, using a subcutaneous skin strip. He reported on it in 1874 and again in 1880. Later Marion used a similar procedure. Two longitudinal incisions are made on the under side of the penis which unite beyond the hypospadias opening. Instead of suturing the skin edges to form a tube, the skin strip is simply buried by wide lateral skin flaps drawn from the sides of the penis and approximated with double interlocking sutures. A dorsal slit is used to relieve tension on the skin flaps and this is allowed to close in with granulations. At another operation the new urethra is anastomosed to the hypospadias opening.

Recently Denis Browne has revived this operation and Burns[4] has also reported results with it. The width of the skin strip is not given but it appears to be so narrow that it is questionable whether a urethra formed in such a manner is of adequate diameter. Experiments conducted by Nesbit[22] with buried skin strips in rats and dogs proved that the tube so formed was no larger in diameter than the width of the skin strip. Although this operation has been acclaimed for its simplicity, it would seem apparent from reading the literature that multiple fistulæ formation is all too common. Also there is some uncertainty as to whether the penis is straight on erection.

2. Urethroplasty using only penile skin is generally called the Thiersch or Thiersch-Duplay operation. It has been modified by Cecil[8, 9] and is excellently illustrated by him. Longitudinal parallel incisions are made on under side of the penis extending from the glans to a point just behind the hypospadias opening where the incisions are joined. The flaps are mobilized and joined with a fine running suture to form the new urethra. The denuded area on the under side of the penis, together with the new urethra itself, is then covered by lateral flaps of penile skin. According to the illustrations, the suture lines lie in different planes. In actual practice this is not easy to achieve. Tension on the suture lines therefore is nearly always present, even though a relaxing dorsal slit is made. Because of tension and proximity of the suture lines, there is a high incidence of multiple fistulæ which are difficult to close. There is also some question whether a urethra so formed is of adequate size. Byars[5] has apparently had more success with this operation than anyone else, and even in his reported cases there were 23% in which fistulæ formed. He did not state the size of the urethra which he had formed.

3. In the Nové Josserand procedure the urethra is made from a free inlay graft. This method was later discarded because of the high incidence of strictures and fistulæ. Recently it has been revived by plastic surgeons, who seem

to be the only ones enthusiastic about it. McIndoe[18] was the first to revive this operation and he was followed by Young and Benjamin[31, 32] and by Havens and Black.[17] The downward curvature of the penis is first corrected and some time thereafter a split-thickness skin graft is taken from an area without hair and sutured around a rubber tube with the raw surface outward. A trocar is passed under the skin of the penis from a point near the hypospadias opening to the end of the penis where it pierces the glans penis. The skin graft is then passed along this tunnel and a dilator left in place for six months or more to prevent contraction of the graft. Later the newly formed urethra is anastomosed at the hypospadias opening. While it is probable that normal diameter of the new urethra is obtained when the dilator is left in place for six months, the graft might be expected to contract longitudinally. This would prevent elongation of the new urethra on erection and some downward curvature would certainly result. This objection applies particularly to the procedure when the graft is placed at the age of two or three as described by Young and Benjamin. It is evident that indifferent results have been obtained with the anastomosis of the new urethra to the hypospadias opening and that many fistulæ have formed which have been difficult to close.

Using this general procedure, Weitz[30] has employed the appendix, Tuffier[27] portions of veins, and Bourque[3] the urethra of a cadaver. Temporary success has sometimes been obtained, but eventually all fail to maintain the desired results. It is well established that autotransplants leave a contracted urethra, unable to elongate on erection, and therefore unsatisfactory for intercourse. Axhausen[1] has shown that homotransplants will eventually be absorbed, leaving only a fibrous cord, or they may be completely extruded as foreign bodies.

4. Urethroplasty by means of the Ombredonne pouch technique[28] has been abandoned because of hair formation in the urethra and stricture and fistula formation.

5. Formation of a urethra from tubes of skin taken from the adjacent scrotum and thigh (Gillies tubes) need barely be mentioned. This procedure uses hair-bearing skin and is subject to frequent stricture and fistula formation.

6. The Bucknall[7] operation in which skin from both the penis and the scrotum is used to form a urethra was the first to employ the principle of embedding the newly formed urethra in the scrotum. This had the distinct advantage of almost entirely eliminating the incidence of fistula formation. The operation has been abandoned, however, because of hair formation in the new urethra.

7. The type of operation which appears most likely to succeed is that in which skin from the under side of the penis is employed in the formation of the new urethra, and scrotal skin as a cover. Penile and preputial skin are ideal for forming the urethra because they do not normally bear hair and are soft and pliable. Moreover, penile skin grows and develops with the penis, and the urethra formed from it will maintain normal length and calibre as the child grows into adult life.

The method for forming the new urethra with skin from the penis is fairly standard. Two parallel incisions are made from the glans penis to the hypospadias opening, and the incisions are united posterior to the urethral opening. A width of skin strip equal to about one-third the circumference of the penis is adequate to form a urethra of normal calibre. Flaps are lifted up on each side and a tube is formed by a continuous suture the length of the incisions.

There are several methods for covering the denuded under surface of the penis with skin from the scrotum. Blair[2] uses an L-shaped flap of skin from one side of the scrotum, and Smith[25] also reports good results from this method. In the Blair operation, however, the new urethra does not incorporate the hypospadias opening and later anastomosis with the new urethra presents some difficulty. Wehrbein[29] prepares a skin tube on the scrotum at the time the downward curvature is corrected. At the time of urethroplasty the skin tube is cut off at its distal end and split longitudinally for use in covering the under surface of the penis. Goodhope[16] and Smith and Blackfield[24] have also reported good results with this operation. On the other hand, my own experience with skin pedicles would suggest that the distal end of the covering flap of scrotal skin obtained by the method of Wehrbein might not have a good blood supply, and this together with the proximity of suture lines would render the procedure more liable to fistula formation than the Cecil operation, which I shall now describe.

Cabot[6] reported this operation first, but gave

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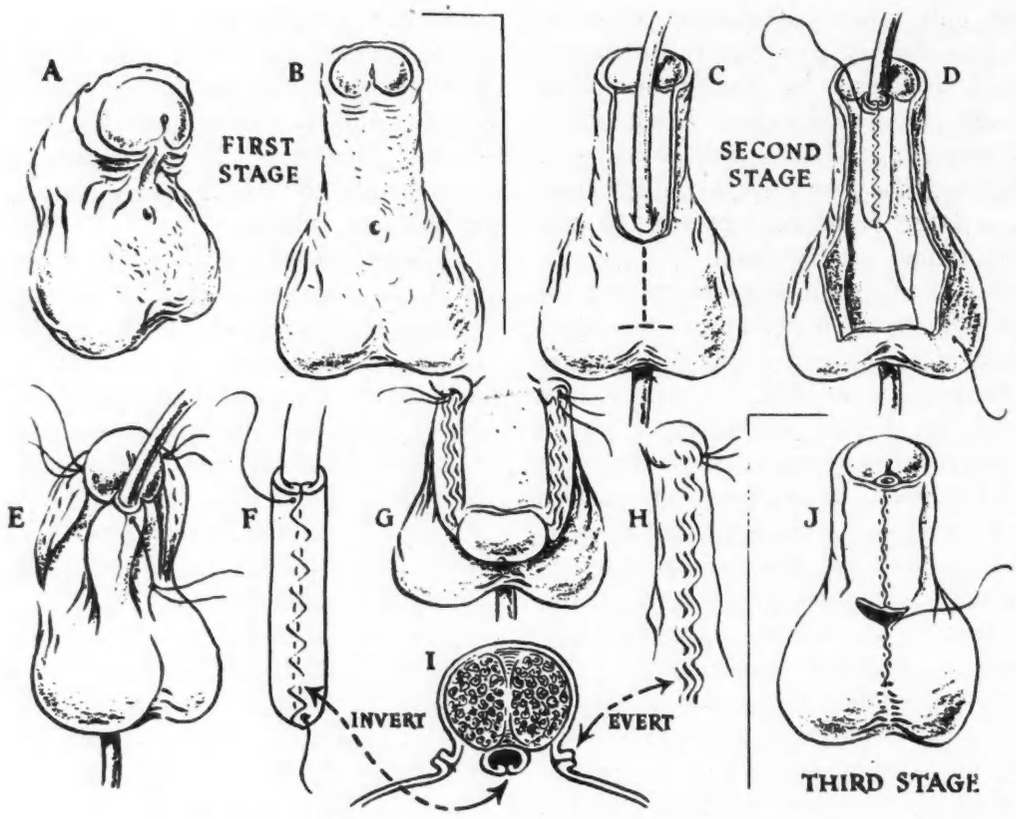

priority to Cecil,[9] who did not publish his article and illustrations until 1946. More recently Culp[12] has reported a series of cases using the Cecil technique. It is this operation which best seems to overcome the difficulties encountered with the preceding techniques.

Urethroplasty may be undertaken whenever it is established that the penis is thoroughly straightened and, in the case of perineal hypospadias, that there are no hair follicles in the skin which is to be used for formation of the extension to the urethra. A careful search must be made with a magnifying glass and if any hair follicles are found they must be destroyed with the diathermy needle. Then, to make sure that they do not regenerate, the surgeon must wait for another six months.

During my early years in practice, when I used the Cecil[8] modification of the Thiersch operation, fistulæ invariably developed. At that time I used catgut for suture material. This irritating substance produces an inflammatory reaction with seropurulent exudate and œdema. It seems that this predisposes to infection and a breakdown of the wound. After Goodhope[16] introduced wire as a suture material in hypospadias operations I substituted this for catgut and immediately obtained good results. But wire kinks easily and is difficult to handle, and its removal after healing is painful. Therefore I have substituted 5-0 Dermalon for wire, since Dermalon does not produce observable tissue reaction, is easy to handle, and is comfortably removed when healing is complete.

The illustration depicts the Cecil technique when applied to penoscrotal hypospadias. It is my opinion that the Cecil principle may be applied to all degrees of hypospadias provided that all hair follicles in skin to be used for urethroplasty are destroyed by diathermy before the operation is undertaken. In two cases of perineal hypospadias I have obtained apparently excellent results, although absence of hair in the urethra cannot be ascertained until after puberty.

The artist's drawing illustrates the Cecil operation as performed by me with use of three Dermalon sutures and a minimum of fine catgut ties on bleeding vessels. Figure A shows a typical penoscrotal hypospadias with downward curvature of the penis. Figure B shows the penis after the downward curvature has been corrected. Figure C shows the strip of skin on the under surface of the penis, about one-third of its circumference, from which the urethra is to be made. The incision lines by which it is to be embedded into the scrotum are shown dotted.

The complete dissection as shown in Figure D should be made immediately so that oozing will have stopped by the time the operation is completed. A single strand of Dermalon suture enters the skin of the scrotum at some distance from the line of incision. This is then

used as an inverting suture to approximate the edges of the skin strip to form a tube extending from the hypospadias opening to the corona (Figs. D and F). The ends of this suture are later tied as shown in Fig. E. When healing is complete it is easy to cut one end and remove it. The scrotal incision is now lifted up as shown in Fig. E and on each side a single Dermalon suture unites the skin of the scrotum to the skin of the penis with a continuous everting suture illustrated in Figs. H and I.

When the operation is complete, the penis is embedded back into the scrotum as shown in Fig. G. There is no tension on any of the suture lines. If much oozing of serum is anticipated, a small Penrose drain may be inserted into the operative area through a stab wound in the scrotum. This can be removed in a few days without fear of fistula formation. No antibiotics are required.

The sutures can be removed in about 12 to 14 days and the perineal urethrostomy or suprapubic cystostomy tube in about three weeks. The patient will then urinate easily through the newly formed urethra, although the penis is still embedded in the scrotum.

After about six months, when the tissues are soft, the penis is dissected from the scrotum with a single midline incision and the skin edges are approximated with a continuous suture as shown in Fig. J.

I have used this operation on 17 patients with uniformly good results. The penis remains straight on erection and the urethra is of adequate calibre and is free from stricture, fistula, and hair formation.

SUMMARY

Satisfactory correction of hypospadias must attain the following objectives: a penis that is straight on erection throughout life, and a urethra free from hair, stricture and fistula, and so situated that urinary and sexual functions are entirely adequate.

The principal methods for correction of the downward curvature of the penis have been described. The principal methods for forming a new urethra have also been described. The shortcomings of many of these operative procedures have been mentioned. The advantages of the Cecil operation and its modifications have been described in some detail. While it is true that the Cecil operation requires three separate stages, only one of them—the formation of the new urethra—requires any prolonged stay in the hospital. The superior functional result far outweighs the disadvantage of multiple stage procedure. It is believed that the wider application of the Cecil method in the future will result in more uniformly good results in the correction of the deformity of hypospadias.

[NOTE: This was Dr. Pilcher's last contribution to medical literature. He died on May 5, 1954. In his covering letter with this article he said that the bibliography will be a valuable source of the world's best literature on hypospadias.—EDITOR.]

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CHOLINE DEPRIVATION AND MUSCULAR DYSTROPHY

The use of vitamin E in the treatment of muscular dystrophy was based on an analogy with the dystrophy produced by tocopherol deprivation in animals. But metabolic and pathologic processes in animals are often misleading guides to those taking place in man, and vitamin E proved useless in human dystrophies.

This group of diseases may be the result of functional neurological disturbances in the muscles, arising from a defect in acetylcholine metabolism. Vitamin E is known to activate the biosynthesis of acetylcholine from choline and acetate.

Hove and Copeland[1] suggest that the fatty peroxides present in vitamin-E-deficient tissues may interfere with acetylation by oxidizing the sulfhydryl group of coenzyme A, a compound essential for the acetylation of choline and acting efficiently only when this group is in the reduced state.

Of greater interest to the clinician is their observation that chronic nutritional deficiency of choline itself can produce, in rabbits, changes characteristic, clinically and pathologically, of progressive muscular dystrophy, even when ten times the normal amount of vitamin E is given. As creatine excretion increases, creatinine excretion decreases. Addition of choline to the diet cures the dystrophy and the creatinuria in three days.

Hove and Copeland[1] point out that the lowering of urinary creatinine is characteristic of human dystrophies, but does not occur in the dystrophy produced in rabbits by deprivation of vitamin E. However, simple choline deficiency cannot be the cause, since stunting of growth and typical liver damage do not occur. Deficiency of any of the nutritional factors (such as pantothenic acid) which are involved in the formation of coenzyme A should likewise produce dystrophic changes.

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OCULAR PENETRATION OF ERYTHROMYCIN

E. I. QUERENGESSER, M.D.* and
H. L. ORMSBY, M.D.,* *Toronto*

SINCE THE ADVENT of the antibiotic age, the ocular penetration of these substances has received attention from various investigators. Unfortunately, many of the most effective antibiotics have proved of little value in the treatment of intraocular infections because of their inability to penetrate into the eye in concentrations sufficient to be therapeutically effective. From the observations of Struble,[1] Leopold,[2, 3] de Roetth,[4] Cannon,[5] and others it is evident that penicillin, streptomycin, aureomycin, and terramycin penetrate the blood-aqueous barrier poorly. Chloramphenicol, on the other hand, has been shown by Leopold[6] and co-workers to penetrate into the eye in good concentrations by most routes. More recently carbomycin has been shown by Halliday,[7] working in this laboratory, to penetrate the blood-aqueous barrier when given topically as the hydrochloride, and by Hausler,[8] when administered by the oral, intravenous, intramuscular, and subconjunctival routes.

Langham[9] has shown that penetration of the blood-aqueous barrier by antibiotics depends on two main factors: upon the size of the molecule, which should not exceed a molecular weight of 500, and upon its fat solubility. While the molecular weight of erythromycin (approximately 725)[10] is above that found to be the maximum for direct penetration, the drug is readily soluble in fat solvents and so fulfils the most important criterion for passing the blood-aqueous barrier.

Erythromycin was the name given to an antibiotic substance produced by the growth of an actinomycete identified as a strain of *Streptomyces erythreus* and was reported by McGuire and associates[10] in 1952. Early reports by McGuire indicated that it was effective *in vitro* against a wide range of micro-organisms. This included the pathogenic Gram-positive bacteria and some of the Gram-negative organisms, such as the neisseria, hæmophilus, and brucella groups. It was also found to be active against certain of the rickettsiæ, and several of the "large" viruses. These findings have been amply confirmed since the early reports and knowledge of the range of susceptible micro-organisms has been extended by Powell,[11] Smith,[12] and others. Kirby[13] and Josselyn[14] made observations on oral administration and found erythromycin to be rapidly absorbed from the upper gastrointestinal tract, giving therapeutic blood levels of 1.0 to 20.0 μgm. per ml. Anderson[15] found it to have few side-effects and extremely low toxicity, and to penetrate readily into most tissues and body fluids.

An important property of erythromycin, demonstrated by Haight[16] and Hobson,[17] was the low incidence of naturally occurring resistant strains of staphylococci. With the exception of carbomycin, cross-resistance with other antibiotics was unusual. Those strains which had become resistant to penicillin and other antibiotics proved to be susceptible to erythromycin. Thus the drug has its greatest usefulness in staphylococcal infections where the organisms have become resistant to other antibiotics. It is equally effective against streptococcal and pneumococcal infections.

Erythromycin* was made available to us for topical application as the crystalline base in white petrolatum and mineral oil (5 mgm./gm.). For subconjunctival administration we used an intravenous preparation of erythromycin base (Compound PR-1, Lilly). The thiocyanate, 50 mgm. per ml. (Compound PR-2, Lilly), was chosen for intramuscular injection.

The eyes of the test animals were cleaned with normal saline and samples of aqueous humour withdrawn by paracentesis with a No. 27 gauge hypodermic needle. Pooled aqueous from the two eyes was used for each test.

The concentrations of erythromycin in the serum and aqueous were determined by a two-fold, serial dilution, turbidimetric bio-assay. The method used was a modification of the technique described by Rammelkamp[18] for the determination of the concentration of penicillin in body fluids. The test organism was a strain of *Staphylococcus aureus* (Peoria) which was found to be sensitive to 0.07 μgm. per ml. of the standard. The tests were subject to the errors of serial dilution procedures in general.

*From the Departments of Ophthalmology and Bacteriology, University of Toronto.

*The erythromycin products used in these experiments were kindly provided by Eli Lilly and Company.

PROCEDURE

1. Seventeen rabbits were treated topically. A small amount of the ointment was placed in the lower conjunctival cul-de-sac every 15 minutes for four applications. The aqueous was withdrawn for assay one hour after the last application.

Results.—This method of application produced average aqueous levels of 1.18 μgm. per ml. of erythromycin, with individual determinations varying from 0.16 to 2.56 μgm. per ml.

2. Five rabbits were given subconjunctival injections of 5 mgm. of erythromycin in 0.25 ml. of distilled water, and seven were given 10 mgm. in 0.25 ml. of distilled water by the same method. Aqueous was withdrawn for assay one hour after injection.

Results.—The subconjunctival administration of 5 mgm. of erythromycin in 0.25 ml. of distilled water gave average aqueous concentrations of 2.43 μgm. per ml., with individual variations of 0.32 to 5.12 μgm. per ml. By the same route, 10 mgm. in 0.25 ml. of distilled water gave average aqueous levels of 5.12 μgm. per ml., with individual variations of 2.56 to 10.24 μgm. per ml.

3. Six rabbits were given erythromycin, 25 mgm. per kg. of body weight, in a single dose by intramuscular injection, and six were given 50 mgm. per kg. via the same route. Serum and aqueous levels of erythromycin were determined on samples taken two hours after injection.

Results.—By this route 25 mgm. per kg. of the drug produced average blood serum levels of 3.01 μgm. per ml., and average aqueous levels of 1.66 μgm. per ml. These determinations showed individual variations of 0.64 to 4.96 μgm. per ml. of serum, and of 0.64 to 2.48 μgm. per ml. of aqueous. By the same method injections of 50 mgm. per kg. gave average blood serum levels of 10.66 μgm. per ml., and average aqueous levels of 3.2 μgm. per ml. The individual variations were from 2.56 to 20.48 μgm. per ml. of serum, and from 1.28 to 5.12 μgm. per ml. of aqueous.

4. Six rabbits were used as controls. No drug was given to these animals. Serum and aqueous samples were obtained for assay as before.

Results.—The serum samples from the control animals showed inhibition of growth of the test bacteria in concentrations equivalent to the activity of 0.021 μgm. per ml. of erythromycin. The aqueous from the control rabbits failed to inhibit the growth in any of the dilution tubes.

TABLE I.

OCULAR PENETRATION OF ERYTHROMYCIN BY VARIOUS ROUTES OF ADMINISTRATION

Route	*Number of tests*	*Dosage*	*Aqueous withdrawn*	*Average levels in μgm/ml.*	
				Serum	*Aqueous*
Topical	17	——	60 min.	——	1.18
Subconjunctival	5	5 mgm.	60 min.	——	2.43
	7	10 mgm.	60 min.	——	5.12
Intramuscular	6	25 mgm./kg.	120 min.	3.01	1.66
	6	50 mgm./kg.	120 min.	10.66	3.2
Controls	6	no drug	——	0.021	0.00

DISCUSSION

The results of these studies indicate that erythromycin passes readily into the aqueous humour of the rabbit. The lowest levels were obtained when the drug was administered topically, producing levels of 1.18 μgm. per ml.; the highest concentration by the subconjunctival route gave 5.12 μgm. per ml. with 10 mgm. of drug. By the intramuscular route 25 mgm. per kg. gave a serum level of 3.01 μgm. per ml. and an aqueous level of 1.66 μgm. per ml.; 50 mgm. per kg. gave blood levels of 10.66 μgm. per ml. and aqueous levels of 3.2 μgm. per ml.

Haight and Finland[19] found that most strains of staphylococci, streptococci, and pneumococci are inhibited by concentrations of erythromycin of 0.01 to 1.56 μgm. per ml. Thus it would appear from the above data that therapeutic levels in the aqueous can be obtained by all three routes of administration.

Kirby[13] and co-workers, using multiple oral dosage with acid-resistant coated tablets, have produced blood levels of not less than 2.0 μgm. per ml. The aqueous levels obtained in our experiments were on the average 30 to 50% of the blood levels obtained when the drug was given parenterally. Therefore it seems that adequate

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aqueous concentrations should be obtained in humans when the drug is administered in suitably coated oral tablets.

SUMMARY

1. Erythromycin ointment applied topically in the conjunctival cul-de-sac of rabbits resulted in average aqueous levels of 1.18 μgm. per ml.

2. Subconjunctival administration of 5 mgm. produced average aqueous levels of 2.43 μgm. per ml., and 10 mgm. gave levels of 5.12 per ml.

3. Intramuscular injection of 25 mgm. per kg. gave serum levels of 3.01 μgm. per ml. and aqueous levels of 1.66 μgm. per ml. By the same route 50 mgm. per kg. gave serum levels of 10.66 μgm. per ml. and aqueous levels of 3.2 μgm. per ml.

4. The controls showed inhibition of growth of the test organism in concentrations equivalent to 0.021 μgm. per ml. of activity of erythromycin in the blood serum. The aqueous in these controls did not inhibit the bacterial growth in any tube.

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VITAMIN D_2 IN DERMATOLOGY

JEAN GRANDBOIS, M.D., F.R.C.P.[C.],
Quebec

ELEVEN YEARS AGO, Charpy[1] introduced vitamin D_2 for the treatment of skin tuberculosis. Many authors have recognized the outstanding value of this therapy. Reports from all over the world, especially from France,[2 to 14] England,[15 to 21] Canada[22 to 26] and the United States,[27] have emphasized the great achievement both scientific and social which that method of treatment represents.

Like other dermatologists who were deeply impressed by these results, I have been interested in using vitamin D_2 in some chronic dermatoses other than tuberculosis.

One hundred and twenty patients, suffering from various skin diseases, were treated with an alcoholic solution of vitamin D_2.* I have included in this series 64 cases reported previously.[26] All these patients were advised to take 600,000 units or 15 milligrams of vitamin D_2 twice a week for the first two weeks and once a week later.

*Radiostol Forte (British Drug Houses).

The patients treated with vitamin D_2 were suffering from the following dermatoses: three from papulo-necrotic tuberculids, four from erythema nodosum, one from sarcoidosis, seven from chronic lupus erythematosus, three from deep mycoses, 16 from acne, nine from lichen planus, 24 from psoriasis, 44 from atopic dermatitis, six from nummular eczema and three patients respectively from pustular psoriasis, parapsoriasis and bacterids. Duration of treatment and results obtained in these cases are summarized in Table I.

The three patients with papulo-necrotic tuberculids were treated for two months, and the outcome was considered excellent in two cases and unchanged in the other. An observation period of a few months confirmed these findings.

All the four patients with erythema nodosum benefited from vitamin D_2. The results were excellent in three cases and good in the other. The effect of this therapy was particularly striking in a chronic and recurrent variety of erythema nodosum.

The only case of sarcoidosis, treated with vitamin D_2 for a month, did not improve; the development of severe digestive disturbances, which

TABLE I.

120 CASES OF SKIN DISEASE TREATED BY VITAMIN D_2

Diagnosis	*Number of cases*	*Duration of treatment (in months)*	*Results*		
			Excellent	*Good*	*Nil*
Papulonecrotic tuberculids	3	2	2		1
Erythema nodosum	4	1	3	1	
Sarcoidosis	1	1			1
Chronic lupus erythematosus	7	2		2	5
Deep mycoses					
Blastomycosis	2	1		1	1
Actinomycosis	1	2			1
Acne					
Pustulosa	13	4	1	10	2
Conglobata	3	15	2	1	
Lichen planus					
Papulosa	7	1½	2	3	2
Hypertrophic	2	7	2		
Psoriasis	24	2½	5	6	13
Atopic dermatitis	44	2	15	23	6
Nummular eczema	6	1½	3	2	1
Pustular psoriasis	1	1			1
Parapsoriasis	1	1			1
Bacterid	1	1			1

were possibly due to vitamin D_2, required the discontinuation of this treatment.

Results obtained in seven patients suffering from chronic discoid lupus erythematosus were negative in five and considered good in two.

The three cases of deep mycoses treated with vitamin D_2 included two of blastomycosis and one of actinomycosis. The case of actinomycosis had not improved after two months of treatment. Of the two cases of blastomycosis, one was slightly improved and the other showed no change after one month's therapeutic trial. Anorexia and a mild depressive state were interpreted as partly due to vitamin D_2 in the last case. The blood urea remained normal, but the blood calcium was 155 mgm. %.

Sixteen patients with acne were also treated with vitamin D_2. Thirteen suffered from acne pustulosa and three from acne conglobata. After four months of treatment, the results were evaluated as excellent in one, good in 10, and negative in two other cases of acne pustulosa.

Vitamin D_2 was successful in the three cases of acne conglobata. In two of these the result was considered as excellent because no active lesions were present after treatment. The other patient had only two or three active lesions. These results were obtained after five or six months, but the resistance of this variety of acne to almost any therapeutic agent makes this new approach worthy of consideration. In one of the successfully treated cases, dihydrostreptomycin was associated with vitamin D_2. These three patients were advised to continue vitamin D_2 for a few months after the disappearance of the lesions.

Nine cases of lichen planus were treated with vitamin D_2. Five of these patients suffered from the usual papular variety and two from the hypertrophic type. In the hypertrophic type the results were excellent after seven months of therapy. Of the patients with the acute papular variety, two were cured, three were very much improved and two did not respond to vitamin D_2. We consider vitamin D_2 a useful drug in lichen planus, particularly the hypertrophic variety.

The 24 cases of psoriasis treated by vitamin D_2 were chronic cases in which the disease had been present from two to 19 years. All of the patients had noticed a great improvement during the summer. Vitamin D_2 given for two months and a half induced complete disappearance of the lesions in two cases and improvement in six; there was no change in 13. Topical treatment did not influence these results, because borated vaseline or salicylic acid 5% in petrolatum was the only medication recommended.

Forty-four patients with atopic dermatitis of an average of 12 years' duration were given vitamin D_2. Topical treatment consisted only of antipruritic lotions or emulsions. The duration of treatment was two months. The results were excellent in 15 cases, good in 23 and negative in six. There is no doubt that vitamin D_2 has a beneficial action in a high percentage of cases of atopic dermatitis.

Six cases of nummular eczema were treated with vitamin D_2. The results were excellent in

three cases, good in two and nil in one after 45 days of treatment. Two patients were free from lesions in three weeks.

No result was obtained with vitamin D_2 in three cases of pustular psoriasis, parapsoriasis and bacterid respectively.

COMMENTS

It is my opinion that vitamin D_2 is a useful drug in some chronic nontuberculous dermatoses. The alcoholic solution is preferred to the oily preparation.

It is interesting to compare the results obtained with vitamin D_2 in these 120 dermatological cases with those reported by other authors.

In cases of papulo-necrotic tuberculids, Huriez and Leborgne,[5] Bureau and Barrière,[8] Goncalves and Peryassu, and Arguello and Consigli[28] reported an equal number of cures and failures. My results were excellent in two cases and negative in one. In erythema nodosum, Comi and Doni[29] consider vitamin D_2 as curative. Three of my four patients responded very well to this therapy and the other was improved.

Some authors[30, 31] have claimed that vitamin D_2 is very successful in the treatment of sarcoidosis. Others[32, 33] have denied the efficacy of this therapy. My only case of Besnier-Boeck-Schaumann disease failed to respond to vitamin D_2. Cases of chronic discoid lupus erythematosus were treated unsuccessfully with vitamin D_2 by Popoff and Inamon[34] and Pascher.[35] In my series of seven patients, no result was obtained in five and some improvement in two.

Raab[36] has reported a case of actinomycosis treated with benefit by vitamin D_2. Of my three patients with deep mycoses, the results were negative in two and good in one.

Of 13 patients suffering from acne pustulosa, I found that vitamin D_2 was very effective in one, helpful in 10 and without effect in two. Three cases of acne conglobata responded very well to vitamin D_2. Similar results have been obtained by Garnier[37] and Strakosch.[38]

Cases of lichen planus have been treated successfully by Charpy,[12] Gaumond,[39] Strakosch[38] and myself.[26] Of the nine cases reported in my series a cure was obtained in two cases of hypertrophic lichen planus. Of the seven cases of the common variety of lichen planus, the results were excellent in two, good in three and nil in two.

Various opinions have been published regarding the value of vitamin D_2 in psoriasis. Some authors[5, 38, 39, 40] observed an interesting response of this dermatosis to vitamin D_2, others[41, 42, 43] did not. In my series of 24 cases, the results were excellent in five, good in six and nil in 13. Without being too optimistic, I believe that vitamin D_2 has a beneficial effect in a certain percentage of cases of psoriasis.

In a previous paper,[26] I reported the successful use of vitamin D_2 in cases of atopic dermatitis. Since that publication, Strakosch[38] reported the marked improvement obtained in 42 of his group of 57 patients treated in this way. Of my present series of 44 patients who have used vitamin D_2 for atopic dermatitis, the results were excellent in 15, good in 23 and nil in six. If we consider the extreme chronicity of this dermatosis and its difficult management, vitamin D_2 may be looked upon as a valuable drug.

Of six patients suffering from nummular eczema, three were cured, two improved and one unchanged after vitamin D_2. As in atopic dermatitis, vitamin D_2 should be used more frequently in cases of nummular eczema.

Barber and Erskine[44] reported two cases of parapsoriasis cured by vitamin D_2. One case of parapsoriasis failed in my hands to improve with the same therapy. One case of pustular psoriasis and another of a bacterid remained unchanged after one month of vitamin D_2.

In my whole group of 120 patients, 111 have been free from any toxic reaction due to vitamin D_2. Some untoward clinical manifestations have appeared in nine patients. Three have developed severe digestive disturbances which required the discontinuation of treatment. Four other patients, after one month of treatment, suffered from mild anorexia which was rapidly controlled after reducing the dose of vitamin D_2. In another case there was some epigastric distress associated with a slight diminution of hearing. One patient complained of blurred vision after three weeks of vitamin D_2. Discontinuation of treatment was followed by rapid disappearance of this symptom.

CONCLUSION

The effect of vitamin D_2 was investigated on 120 patients suffering from varied dermatoses.

The results attained in erythema nodosum, acne pustulosa and conglobata, in lichen planus, in atopic dermatitis and in nummular eczema were very encouraging.

Cases of papulo-necrotic tuberculid and psoriasis responded in certain instances to vitamin D_2.

The drug appears to have no value in the treatment of sarcoidosis, chronic lupus erythematosus, deep mycosis, pustular psoriasis, parapsoriasis and bacterids.

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22 Place d'Aiguillon.

Case Reports

CHRONIC TOPHACEOUS GOUT

M. G. P. CAMERON, M.D., F.R.C.P.[C.],
Saskatoon, Sask.

THE VARIOUS MANIFESTATIONS of gout account for 1.5 to 3% of all cases of arthritis.[1] It is not a rare disease, the average practitioner seeing one or two cases per year. Most of these will be examples of acute gouty arthritis, with one or more attacks of acute podagra annually. Definitive treatment at this stage will often prevent the development of chronic tophaceous gout with its severe deformities and terminal renal failure. The patient whose case is described below died after many years of invalidism, but little attention had been paid to his symptoms in the early stages. Although it cannot be proved, it is reasonable to assume that persistent treatment in the acute phase would have lessened the chances of the chronic state developing.

All gouty subjects show hyperuricæmia, although not all the symptoms of gout can be explained on the basis of an error in purine metabolism.[2] Genetic studies[3] have shown that hyperuricæmia is transmitted by a single dominant autosomal gene which is not sex-linked. Gout becomes manifest in only a small percentage of these individuals, the proportion in men being much higher than in women. The blood uric acid level in non-gouty males is higher than that in non-gouty females. Gout rarely appears before puberty in males and before the menopause in women, and the average age at onset is younger in males.[4] Gout appearing in young individuals, generally speaking, is more severe than when it first makes its appearance in the older age group. The reasons for these various observations are not understood.[5, 6]

PURINE METABOLISM

Studies with N^{15} labelled uric acid precursors[4, 7] have yielded valuable information concerning the intermediary metabolism of uric acid in gouty and normal individuals. High blood uric acid levels may result from either (1) overproduction of urates from exogenous and endogenous sources; (2) increased breakdown

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of nucleic acids; or (3) decreased urinary excretion. In some instances there is an overproduction of urates; these urates are formed directly from glycine and other simple compounds which normally metabolize to urea. N^{15} from labelled glycine appears in the excreted urate of some gouty subjects faster than in normal ones, indicating that the urate is formed directly from glycine rather than after intermediary incorporation of the N^{15} into nucleic acids. This metabolic variant causes an elevation of blood uric acid in some but not all gouty subjects.

The second theoretical cause of high blood uric acid levels, namely, increased rate of breakdown of nucleic acids, has no experimental evidence to support it.[4] However, endogenous nucleic acids do break down slowly into uric acid as well as urea. These nucleic acids are not wholly dependent on dietary purines for their formation. Nevertheless in gouty subjects there may be increased production of nucleoproteins from dietary purines. On a low purine diet a normal man excretes 0.3 to 0.5 gm. of urates per 24 hours through the kidneys. This quantity is exceeded in some gouty subjects, and after a high purine meal it may be increased by 100%. It follows that, although diet will not control blood uric acid levels and excretion rates, the ingestion of excess amounts of purine would put a strain on the excretory mechanisms, and excess urates might be precipitated out of solution in the tissues, with formation of tophi.

The third theoretical cause of high blood uric acid levels has also been studied.[8] In young gouty individuals there is no decrease in urate clearance in comparison with the normal. Glomerular filtration of urate is complete and there is tubular reabsorption of all but 5 to 10%. This is accomplished by an enzymatic transfer mechanism whose exact nature has not been identified. Impairment of kidney function occurs late in the disease and is due to direct damage to kidney parenchyma by urate deposits.

MANAGEMENT

The treatment of chronic tophaceous gout is aimed at (1) reducing the deposits of urate by increasing the excretory rate; and (2) decreasing the formation of urate so far as possible by restricting the intake of purines in the diet. This second factor has already been discussed.

Agents which are useful in preventing tubular reabsorption of urates, and therefore increasing urate excretion (uricosuric agents) are salicylates, carinamide,[9] probenecid (Benemid) and ACTH or cortisone.[7] The dosage of salicylates necessary to maintain high uricosuria is toxic to most patients after a variable length of time. ACTH is a good tubular blocking agent, but its other effects are too numerous to allow of prolonged use in the required dosage. Oral cortisone has similar disadvantages and is less reliable as an uricosuric agent. Carinamide is less effective than probenecid, which is considered to be the most specific and least toxic of all agents studied. It has been pointed out[10] that salicylates completely nullify the effect of probenecid, and the two agents should not be used together. The average dose of probenecid is 2 gm. daily in divided doses.

The following case is presented first of all to show the striking degree of deformity which may occur in gout and, secondly, to show the failure of treatment at this advanced stage of the disease.

R.C., a 34-year-old male, was admitted to the Saskatoon City Hospital with a request that his hands be amputated because of loss of function and pain.

His first attack of pain in the great toe occurred when he was 12 years old. It lasted three days and was typical of the severe pain of acute podagra. Six months later the other great toe was similarly affected. Further attacks occurred over the next eight years with increasing frequency. They became less amenable to therapy and lasted as long as 14 days. At the age of 20, pain and swelling occurred in the index and fifth fingers of the left hand. After a week the pain subsided but the swelling persisted. One year later, nodules appeared on his ears and these subsequently ulcerated. The right wrist joint was the site of an acute attack at that time and this was followed by involvement of the other hand, the tarsal joints, the knees and the elbows. When he was 24, surgical drainage of a tophus overlying the right knee joint was carried out. Drainage continued for six weeks. When he was 31 years old he was totally bedridden, due to destruction of knees and ankles by the tophaceous process. One year later he could not feed himself, he became emaciated and many of the ulcerated tophi were secondarily infected. He required periodic blood transfusions because of severe secondary anæmia. He was previously told that his kidney function was too poor to permit the use of cortisone.

Three members of his family (father, brother and sister) were told that the pains they had in their toes were due to gout. These occurred during their teens and they are all free from symptoms at present.

Examination revealed extreme emaciation. The patient was lying almost immobile, with elbows and knees ankylosed in flexed positions. Large numbers of tophi were present on the ears and limbs. Many of these were ulcerated, and white, chalky material could be scraped from their bases. Some of them lay directly over elbow, knee, ankle and hand joints. Both elbows were fixed at 90° of flexion. The knees had about 15° of movement, from 90 to 105°. The wrists, hands and fingers were flexed into immobile half-clenched fists and foul-smelling pus was pouring out of the numerous ulcerations between the fingers (Fig. 1).

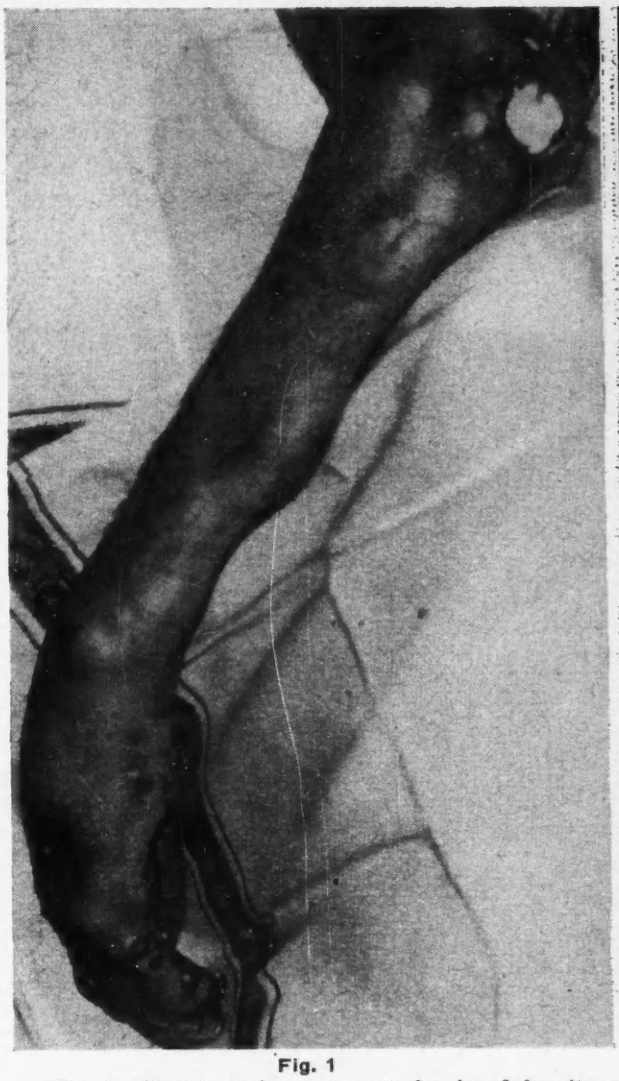

Fig. 1

Fig. 2

Fig. 1.—Chronic tophaceous gout showing deformity of hand and ulcerating tophi. **Fig. 2.**—Same case. Radiograph on hand showing total destruction of carpus, pathological fractures of metacarpals and subluxations of terminal phalanges.

The hæmoglobin was 8.0 gm., the red cell count 2.3 million, the white cell count 6,050 with 41% neutrophils, 15% rhabdocytes, 31% lymphocytes, 7% monocytes and 1% eosinophils. Urinalysis revealed a trace of albumin and specific gravity ranging from 1.005 to 1.007. Blood non-protein nitrogen (NPN) was 46 mgm. per 100 c.c. The serum uric acid was 8.6 mgm. per 100 c.c. The total protein was 6.0 gm. per 100 c.c. with 3.8 gm. globulin and 2.2 gm. albumin. The calcium was 8.5 mgm. and the phosphorus 5.6 mgm. per 100 c.c. The alkaline phosphatase level was 4.5 King and Armstrong units. Material from several ulcerating tophi was identified chemically and microscopically as sodium monourate. A Congo red test for amyloidosis did not reveal any abnormal retention of the dye.

X-ray examination of the hands revealed severe decalcification with fractures of several phalanges (Fig. 2). The tophi contained little or no radio-opaque material.

After initial investigation the patient was started on probenecid (Benemid) 2.0 gm. daily for 10 days, and oral cortisone, 967.5 mgm. in 17 days. He became buoyant in spirit and developed acne and moon facies. The ulcers were cleaned up with antibiotic therapy both locally and by mouth. The urinary output of urates was estimated as 1.1 gm. in 24 hours. Unfortunately, salt and water retention occurred, his NPN rose to 175 mgm. per 100 c.c. and his urinary output fell to 200 c.c. in 24 hours. Medication was stopped and kidney function partially recovered, the NPN dropping to 75 mgm. per 100 c.c. One week after cessation of therapy the urate excretion was only 0.6 gm. per 24 hours. Bronchopneumonia developed about this time with no febrile response and he died 24 hours later.

At autopsy* the bronchopneumonia was confirmed. The right kidney weighed 39.5 gm. and the left 65.0 gm. Deposits of tiny, irregular brownish-grey concretions up to 0.3 cm. in diameter were present in both pyramids and calyces. The cortex was compressed by the urate deposits to a shell 0.3 cm. in thickness in some areas while in other areas it was swollen to about 2 cm. (Fig. 3). Microscopically there was a foreign-body giant cell response and reactive fibrosis about the crystalline material deposited in the interstitial tissues. The renal parenchyma, apart from the reaction to sodium urate deposits, had sustained widespread non-specific chronic inflammatory damage. There was glomerular hyalinization and fibrosis with associated tubular destruction and atrophy and increase in interstitial tissue. The kidney pelves also showed evidence of severe chronic pyelonephritis. Sections through the right metatarso-phalangeal joint revealed the long needle-like urate crystals arranged radially around a central hub as well as deposited in large irregular

*Performed by Dr. J. W. Adams, Pathologist, Saskatoon City Hospital.

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masses. Old and recent hæmorrhages and collections of lymphocytes, plasma cells and histiocytes were seen in the periarticular tissues, the joint itself being completely destroyed.

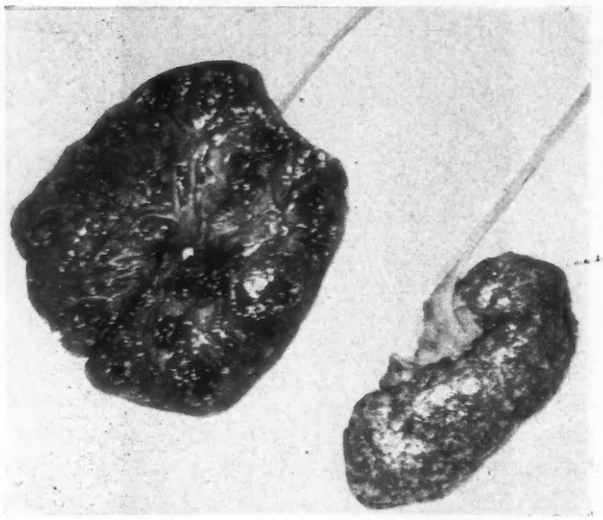

Fig. 3.—Appearance of kidneys at autopsy showing widespread urate deposition and irregular destruction of cortical tissue.

COMMENT

Talbott[11] described a case (Case 1) similar to this one in which the feet were amputated to alleviate pain. It is extremely doubtful whether any form of treatment would have benefited our patient even if renal failure had not occurred. However, it is worth describing such a case to suggest that early treatment may prevent the development of an advanced state.

This patient's illness was diagnosed 20 years before his death. His father was told he had gout when he was in his teens and he recovered. Two other members of the family also are said to have had gout and are now alive and well. The course of the disease can be extremely variable, and the patient no doubt was reassured that his disease would "get better itself." Vigorous treatment was not attempted until he realized that he was becoming crippled. A satisfactory uricosuric agent was not available at that time and he went on to prolonged invalidism. The use of colchicine and salicylates has been quite satisfactory in suppressing acute attacks. Cinchophen has been used with caution in chronic cases because of its frequent toxicity. Considerable promise is being given that nontoxic uricosuric agents such as probenecid may be used for long periods of time. If their use is instituted during the acute phase, the development of chronic tophaceous gout may be prevented.

SUMMARY

1. A fatal case of chronic tophaceous gout with renal failure is presented.

2. Some of the newer experimental data on uric acid metabolism are summarized.

3. The rationale of treatment with uricosuric agents, as used in this case, is outlined and the reasons for failure are noted.

4. A plea for more persistent therapy in the acute phase is made, because this is the only known way of preventing development of such crippling deformities as are seen in this patient.

I wish to thank Dr. W. D. Brace for referring this case and encouraging me to publish it.

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1032 Spadina Crescent East.

NON-TUBERCULOUS SPINAL EPIDURAL ABSCESS*

FELICIA D. HUTCHINSON, M.B., B.S.,
Kingston, Ont.

THERE ARE A NUMBER of obscure places in which blood-borne infection may settle and lurk, often for days, without giving rise to a characteristic clinical syndrome. One thinks of perirenal abscess, lung abscess, brain abscess and subdiaphragmatic abscess. This case is presented as an example of infection and suppuration in another hidden place, the epidural space, the recognition and treatment of which is an urgent matter if an unfortunate or fatal outcome is to be avoided.

On January 20, 1954, a 4 year old girl was referred to hospital for investigation of pain in her left thigh and a raised temperature for three days.

She had been perfectly well until January 17, three days before admission, when she vomited once, lost her appetite, was feverish and wanted to sleep a great deal. The next day, she developed a sore throat and was seen by her doctor and given sulfadiazine. The day before

*From the Department of Pædiatrics, Queen's University, Kingston, Ont.

admission, she was still feverish, would not eat and complained of pain in her left thigh which was aggravated by movement.

The child had had impetigo one month before and measles and tonsillitis six months before, and frequently suffered from infected cuts and paronychiæ.

She was thin and flushed, looked ill, and had a rectal temperature of 104° F. The tonsils were injected and some small cervical lymph nodes were palpable. The skin was normal and examination of the abdomen and central nervous system was negative.

She pointed to the outer side of the left thigh, over the upper part of the shaft of the femur, as the site of the pain, but no swelling, redness or local tenderness was detected. There was no shortening of the left leg and no wasting of the thigh muscles. Extreme flexion and abduction of the left hip were limited by pain but other movements were full and painless. Trendelenburg's sign was negative. She could just touch her toes and there was no local tenderness on percussion over the spine. She walked with a slight limp, with her hand supporting her left thigh at the site of the pain. Examination of the other systems disclosed no abnormality.

A provisional diagnosis was made of mild upper respiratory infection and a lesion in the left hip joint, either tuberculous or acute osteomyelitis. She was observed for the next 24 hours. Blood examination showed an Hb value of 11 gm., white blood count of 11,000, with 78% neutrophils and 16% lymphocytes and erythrocyte sedimentation rate of 69 mm. in 1 hour. Radiography of both hips, femora and the lumbar spine revealed no abnormality. The Mantoux test at 1:2,000 and 1:100 was negative.

The following day, January 21, she was still ill, with a temperature between 103 and 105° F. She was drinking well and not vomiting. Her white cell count had risen to 14,900 and neutrophils to 85%.

A provisional diagnosis of acute osteomyelitis of the left femur was entertained and treatment was started with crystalline penicillin 250,000 units every 4 hours and sulphadiazine 0.5 gm. every 4 hours.

By the 4th hospital day she had not improved, her temperature was still between 103 and 104° F. and she was listless. She was complaining of pain across her abdomen but there was no tenderness or guarding on palpation. Streptomycin 0.5 gm. b.i.d. was added to the treatment. On the 5th hospital day she complained of a headache for the first time, and had some neck stiffness and a positive Kernig sign, but there were no other abnormal neurological findings. A lumbar puncture was attempted twice in the space between L 3 and 4 and once between L 2 and 3 and, though the needle appeared to be in a satisfactory position, no CSF was obtained. Very gentle aspiration with a syringe attached to the L.P. needle was then tried and about 2 c.c. of very thick, creamy pus was obtained. Culture yielded a pure growth of coagulase positive staphylococci sensitive to chloramphenicol, aureomycin, erythromycin and streptomycin. A cisternal puncture was performed and macroscopically clear fluid was obtained. There were 162 neutrophils and 39 lymphocytes and it was sterile on culture.

A diagnosis of spinal epidural abscess was made and the child had an exploratory laminectomy on the 7th hospital day. On the morning of operation, the left plantar response was extensor for the first time. There were no other neurological abnormalities.

The lower four lumbar vertebræ were exposed through a midline incision. The lower half of the right lamina of the third lumbar vertebra was nibbled away and the ligamentum flavum partly excised. Exploration of the extradural space reached pus. A fine ureteric catheter was then passed upwards until resistance was encountered. It was thought that this took place about the level of the tenth thoracic vertebra. The lower border of the left fourth lumbar vertebra was then nibbled away and the ligamentum flavum removed. A fine ureteric catheter was passed downwards to about the level of the middle of the sacrum. The extradural space was washed out with saline, after which 500 mgm. of terramycin was instilled and the wound was closed in layers around the catheters.

Following operation she was given erythromycin 100 mgm. every six hours, and terramycin 500 mgm. was instilled into both catheters daily. The day following operation, the left plantar reflex became flexor. Four days after operation her temperature was within normal limits and her general condition was greatly improved. Eight days after operation the antibiotics were deliberately changed to Chloromycetin palmitate 125 mgm. every six hours and streptomycin 0.5 gm. into the catheters. This was done to eliminate any organisms which might have become resistant to the antibiotics previously used. The wound healed well and the catheters were removed 20 days after operation. By the 13th postoperative day she could walk a few steps with support but lacked confidence to stand by herself. However, with physiotherapy she showed rapid improvement and, at the time of her discharge on February 28, 32 days after operation, she was running and playing normally with the other children and had no abnormal physical findings.

She was seen again 7 weeks after the operation, when she appeared perfectly well, but her mother had noticed that the left foot was much colder than the right. The left foot was cold and clammy and this was thought to be due to autonomic disturbance following pressure and infection in the epidural space.

DISCUSSION

The primary focus of infection is frequently a minor cutaneous infection such as acne or a boil. In some cases the epidural abscess is secondary to an acute osteomyelitis of a vertebra, and some cases have been described following a lumbar puncture. There is often a history of trauma, such as a fall on the back. *Staphylococcus aureus* is the usual causative organism, though infections with the pneumococcus and streptococcus have been reported.

This lesion is by no means a rarity. Heusner reviewed 20 consecutive cases of non-tuberculous spinal epidural abscess seen between 1930 and 1948. He classified them as acute spinal epidural infections, running a rapid clinical course, and chronic infections which develop insidiously. Both types of infection have a similar clinical pattern which is as follows: Phase I, spinal ache; Phase II, root pain; Phase III, weakness of voluntary muscles and sphincters, sensory disturbances; Phase IV, paralysis.

The case described was first seen in Phase II and, on the morning of operation, was showing the first sign of pyramidal tract involvement. It is important to consider the possibility of a spinal epidural abscess in patients with an unexplained fever, pain and tenderness over the spine, or root pains as the lesion should be treated as a surgical emergency and exploratory laminectomy carried out immediately. This is necessary because the transition from Phase III to IV may be very

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short, taking only a few hours, and once paralysis has occurred the changes are usually irreversible. Heusner describes complete recovery in all patients who had no paralysis or paresis of less than 36 hours' duration at the time of operation.

In a recent paper, Hulme and Dott reviewed 20 cases that had come under their care. They also stressed the importance of immediate operation once the diagnosis has been made. If surgical drainage of the abscess is performed and antibiotic therapy is started before there is any gross neurological abnormality, complete recovery may be anticipated.

The case described was unusual in that the child never complained of any spinal ache, and there was no tenderness even on light percussion over the vertebræ.

A partial rather than complete laminectomy was performed as in children it is desirable to preserve the laminæ to prevent kyphosis later.

CONCLUSION

A case of non-tuberculous spinal epidural abscess is described, in which the diagnosis was made before the onset of paralysis.

There was complete recovery following drainage of the abscess and antibiotic therapy.

My thanks are due to Dr. D. L. C. Bingham, Professor of Surgery at Queen's University, for assistance in presenting this case.

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SEVEN RECURRENT ATTACKS OF PNEUMOCOCCIC MENINGITIS WITH RECOVERY*

PERCY BARSKY, M.D., *Winnipeg*

PNEUMOCOCCIC MENINGITIS was almost universally fatal before penicillin and sulfonamide therapy. As late as 1944, Waring and Smith[1] reported 150 cases from the Harriet Lane Home in Baltimore, among which there were no recoveries. The disease was almost invariably fatal at the Children's Hospital of Washington, where, in 1946, Ross and Burke[2] described one recovery in 66 patients. All of the 157 patients observed by Toomey and Roach[3] of Cleveland in 1937 succumbed.

Recent advances in therapy have dramatically influenced the fatality rate in pneumococcic meningitis, and penicillin gives better results in this disease than any other therapeutic agent.[4] The purpose of this paper is to report a case of seven recurrent attacks of pneumococcic meningitis with recovery in a 4½-year-old boy.

First admission.—At 2 a.m. on December 5, 1952, this child was admitted to the Children's Hospital. He was found at 2.30 a.m. on November 27, 1952, at the foot of a flight of stairs. Apparently he had fallen out of his crib. He then complained of pain at the back of his head and remained dazed for an hour. He vomited immediately after and three times during the next 12 hours. During the following day he vomited several times. The next morning he awoke at 7 a.m. complaining of pain in his right ear. He had an elevated temperature and was both irritable and drowsy. This was followed by a period of disorientation, and he was then admitted.

Upon admission, this pale, lethargic, irritable boy of 4½ years appeared grossly disorientated. His head was thrown back in moderate opisthotonos. The pupils were miotic and equal. The fundoscopic examination was negative. The patient resented examination of his left ear; both drums were visualized with considerable injection. The posterior pharynx was fiery red and there was much clear mucoid material at the back of his throat. His chest movements were poor and his respirations were abdominal. Diffuse rhonchi were heard throughout his chest. His abdomen was soft, but the patient resented abdominal examination. The blood pressure was 130/80, and pulse rate 140. Deep and superficial reflexes were all bilaterally normal. There was marked nuchal rigidity and Kernig's sign was positive.

Laboratory studies revealed a grossly purulent spinal fluid which contained 1,370 white cells, 85% of which were polymorphonuclears. The spinal fluid protein level was 50 mgm. % and sugar 51.5 mgm. %. Culture of this fluid showed Gram-positive diplococci resembling pneumococci. The throat swab grew a profuse strain of *Diplococcus pneumoniæ*. The blood count was 4,500,000; hæmoglobin value 13.8 gm.; white cell count 22,850.

Shortly after being admitted the child was given 1,000,000 units of crystalline penicillin intravenously along with 1½ gm. of Soludiazine. Four hours later 500 mgm. of aureomycin was given and repeated every four hours. The aureomycin was stopped within 24 hours and the penicillin and Soludiazine were continued for one week.

In less than 48 hours his temperature had subsided and improvement began. No growth was obtained on blood culture, but throat swabs demonstrated the presence of a few colonies of *Diplococcus pneumoniæ*. Lumbar puncture on December 2 showed a clear cerebrospinal fluid at normal pressure. Neurological and physical examination were negative on this date.

Second admission.—On January 31, 1953, the child developed a temperature of 103° F. and seemed to have a head cold. He was given steam inhalations and appeared to improve until the night previous to admission (February 3), when he awoke screaming and holding the top of his head. His arms and legs and then his neck developed stiffness. At about this time he had a nosebleed. He had no convulsions, nor had he fainted at any time. He had been suffering from headaches for the past 12 hours. He had pains in his legs off and on since his discharge from this hospital in December. His mother stated that this present attack differed from the previous in that (a) there was no history of trauma; (b) there was no nausea or vomiting; (c) the child was not drowsy as previously.

*Children's Hospital, Winnipeg, Manitoba.

The boy was in considerable discomfort, lying curled up on his right side. His head was drawn into a position of acute opisthotonos; his right ear was painful on examination and there was marked neck stiffness. His chest was resonant and the breath sounds were vesicular. His blood pressure was 110/70 and his pulse regular. No murmurs were detected and there were no masses palpable in his abdomen. There was questionable right lower quadrant tenderness and his legs were drawn up in a position of semi-flexion. He had a bilaterally positive Kernig's sign. Lumbar puncture revealed a cloudy cerebrospinal fluid containing 19,000 white cells of which 93% were polymorphonuclears. The spinal fluid protein level equalled 260 mgm. %, chlorides 115 mgm. and sugar 10 mgm. %. In smears of the cerebrospinal fluid no organisms were seen. Culture yielded a colony of pneumococci in 48 hours. The spinal fluid was incubated, and many Gram-negative diplococci were present. The blood culture taken on February 7 showed no growth.

Following the initial lumbar puncture, he was given 1,000,000 units of crystalline penicillin in 300 c.c. of 5% glucose intravenously and 1 gm. of Soludiazine; 0.75 gm. Soludiazine was given every four hours and 500,000 units of crystalline penicillin six times daily for two days. Then the child was placed on 300,000 units of repository penicillin every four hours. During the whole course, sulfadiazine in two-gram doses every four hours was administered. On February 12, the sulfadiazine was stopped. A lumbar puncture was performed on February 14, and the count at this time showed 62 cells, 80% being lymphocytes. The total protein was 40 mgm. % and the pressure initially was 200 mm. of water. On February 18, the lumbar puncture was repeated and 30 cells, 65% being lymphocytes, and 32 mgm. % protein were reported. The clinical response this time was slightly slower than during the previous admission but on discharge the boy showed no clinical signs relative to his previous infection. On March 2, the patient was discharged from hospital.

Third admission.—The boy's third admission occurred on March 24, 1953. He complained of a running left ear since March 22, and pain in the left ear for the past 18 hours. Apparently he had been vomiting and had a very severe headache since 6 a.m. on March 24. Both ears had been infected for the past three weeks and on March 22, the left ear drum had ruptured. Since 6 a.m. on March 24, the patient had been lethargic and drowsy and had incoherent speech. His temperature was 103.4° F. His left ear was discharging profusely, but the right ear was normal. There was some serous discharge from his nose. A lumbar puncture was done and a few c.c. of cloudy cerebrospinal fluid was removed. He was placed on 1,000,000 units of crystalline penicillin every four hours and no other antibiotics were given at that time. The penicillin was maintained for a week.

The cerebrospinal fluid on March 25 grew Gram-positive diplococci; it contained 1,040 white cells, 83% polymorphonuclears, and the protein equalled 110 mgm. %. March 31, it showed 41 white blood cells, 90% of these being lymphocytes. On April 16 there were 9 white cells in the spinal fluid and there was no growth on culture. His initial white cell count was 12,150 and his urinalysis was negative. A chest film showed minor tuberculous infiltration in the right lung. Radiographs of both mastoids showed a fair amount of sclerosis. A pneumoencephalogram was essentially normal. The vertebral column showed no abnormality apart from a rather prominent cervical lordosis. He was discharged from hospital on April 20, 1953, with no evident signs.

Fourth admission.—This boy's fourth admission was on May 7, 1953. He again complained of headache, stiff neck, and vomiting which began on this date. Apparently he had been well until 1 p.m. of the date of admission, when suddenly he began to complain of a headache and of pain in his right ear. He vomited, his neck was rigid, he was very irritable and drowsy, and he looked quite ill. A lumbar puncture was done and several c.c. of opalescent fluid was removed. The right ear drum was red and bulging. The boy appeared quite ill and showed gross signs of cerebral irritation, as on the previous admission. He was almost semicomatose, his reflexes were hypertonic, his neck was rigid, and he was delirious.

After his lumbar puncture was done and blood taken, he was given 1,000,000 units of crystalline penicillin intravenously, and 500,000 units of penicillin were ordered every four hours together with 0.5 gm. of Soludiazine for the next 48 hours. Then crystalline penicillin in 500,000 unit doses every 4 hours was instituted and sulfadiazine was given by mouth. By May 10, crystalline penicillin was given intramuscularly in dosage of 100,000 units every six hours and this was continued for the next four days. Chemotherapy was terminated on May 18 except for penicillin, which was maintained at 300,000 international units every six hours for the next week. Following this, penicillin in doses of 300,000 units twice daily for the next six days was given.

His initial lumbar puncture on May 7 showed a protein level of 160 mgm. %; a smear of the spinal fluid showed pus with pneumococci and there were 6,200 white cells. On May 8, the culture in the laboratory grew pneumococci. By May 12, the protein level in the cerebrospinal fluid had gone down to 48 mgm. % and the white cell count totalled 76 cells of which 33% were polymorphs. His hæmoglobin value was 11.4 and his white cell count 10,600. By May 8, he had improved considerably and there was no further drowsiness. By May 11, no lesion of the cranial nerves was detected, there was no muscle weakness, and it was evident at that time that he had hypertrophic adenoids. By May 13, his spinal fluid showed only 16 white cells. His condition appeared satisfactory and radiography of both mastoids was again repeated. This showed a recent infection in the right mastoid air cells. On May 26, an adenoidectomy was performed. On June 4, 1953, a simple right mastoid scraping was done. On June 15, 1953, the patient was sent home.

Fifth admission.—At 11.45 p.m. on July 5, 1953, the boy was admitted for the fifth time. Again the complaint was of a severe frontal headache associated with projectile vomiting since 9 p.m. on July 5. The temperature on admission was 102° F. His neck was extraordinarily stiff, and Kernig's sign was positive. There was minimal injection of the right ear drum and this time he had a systolic apical murmur, which had not been heard previously. The lumbar puncture showed 12,400 white cells, of which 90% appeared to be polymorphonuclear. The smear was positive for pneumococci. In spite of the fact that he was almost moribund on this admission, the response to specific antibiotic therapy was most gratifying. He was given a million units of crystalline penicillin intramuscularly and one million units intravenously immediately after his lumbar puncture and blood sampling had been done. He was maintained on 500,000 units of crystalline penicillin every four hours as well as 7½ grains (0.5 gm.) of Soludiazine intravenously every four hours for the next five days, and then repository penicillin in doses of 400,000 units every four hours for ten days along with the previous Soludiazine dosage. By July 7, 1953, his temperature had come down to 99° F., he was no longer opisthotonic and responded to external stimuli, and he appeared to be at least on the road to recovery. By July 15, 1953, he was discharged on 1,200,000 units of long-acting dibenzylethylenediamine dipenicillin G. His parents had been advised to bring him back weekly so that penicillin prophylaxis could be carried on together with penicillin level determinations in spinal fluid.

Sixth admission.—The boy's sixth admission occurred on October 7, 1953, at 7.15 a.m. Apparently the child had awakened on the night of October 6 with a severe frontal headache, had vomited, and was in a semicomatose state. On examination he had swollen cervical nodes, a stiff back, and a red throat. His white cell count was 53,000 and spinal fluid smear showed no organisms. The spinal fluid protein level was 420 mgm. %, sugar 17.6 mgm. %, and culture grew pneumococci. His chest movements were equal, there was no indrawing; his pulse was 140 and regular. Lumbar puncture was done

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and pneumococci were demonstrated on spinal fluid smear. Then penicillin was given in doses of two million units every two hours, with one gram of Gantrisin every six hours. His skull films were repeatedly negative and it was not possible to demonstrate a fracture line. Sinus films were taken, his whole spine was radiographed, and his mastoids were again radiographed; all of these were non-contributory. His head was shaved and a congenital dermal sinus searched for in vain. His cerebrospinal fluid on admission grew pneumococci. Blood culture was repeatedly negative. He was kept on large doses of penicillin and penicillin assays were done. He was finally placed on two million units of oral penicillin G twice daily. This gave him a cerebrospinal fluid level of 0.03 unit penicillin per ml. and serum level of 2.0 units penicillin per ml. On December 24, 1953, he was sent home on prophylactic oral penicillin G, in doses of one million units four times daily. The boy was kept on this dose of penicillin after discharge and was seen repeatedly in the out-patient department.

Seventh admission.—This occurred on April 12, 1954. The boy had been on four million units of oral penicillin G since his sixth attack. His father stated that on April 6, 1954, they ran out of penicillin. At 8.30 p.m. on April 12, he awoke complaining of severe frontal headache and in an oculogyric crisis. He vomited and was promptly brought into hospital. He was semi-comatose again and delirious. There was marked nuchal rigidity and a positive Kernig's sign, and deep tendon reflexes were all accentuated. There were no petechiæ. Ophthalmoscopic examination was negative. Cerebrospinal fluid showed 2,826 cells, 90% being polymorphs, and the smear was positive for pneumococci. Cerebrospinal fluid protein equalled 95 mgm. %, sugar 34.2, and chlorides 120.6. He was placed on one million units of penicillin every two hours and one gram of sulfadiazine every six hours for the next five days. The penicillin was then cut to one million every four hours for three days, and subsequently he was on oral penicillin in a dosage of two million units twice daily. By April 30, he had clinically recovered. Search for a congenital dermal sinus was again fruitless. On May 9, a tonsillectomy and exploratory right mastoidotomy were performed. Culture of the tonsillar tissue showed streptococci and staphylococci, but no pneumococci. He was discharged on May 11, 1954, on 500,000 units of oral penicillin G twice daily and this dosage is being maintained. He is seen weekly at the regular follow-up clinic and is symptom-free.

DISCUSSION

No condition better reflects the advances in the field of antibiotic therapy during the past 15 years than does pneumococcic meningitis. This disease until 1936 was almost invariably fatal, and prior to this date there were only 185 reported cures.[5] Since 1937 there have been 25 papers describing one to three case reports of recurrent meningitis.

Bronstein[6] reported the case of a man who had four attacks of meningitis in a period of eight years. On two occasions the illness was attributed to the meningococcus. Craddock and Bowers[7] described the case of a woman who had four attacks with recovery. On the first occasion Type 17 pneumococci were identified. During the second attack the spinal fluid was sterile, and the third time Type 18 pneumococcus was identified. The fourth attack again showed a sterile spinal fluid.

Hoyne[8] reported three patients with second attacks of pneumococcic meningitis occurring at intervals of about six months to one year. In each case the infecting organism was of a different type in the two attacks. Traut[9] had a patient who had meningitis five times with recovery, and in this case there was a history of skull fracture two years previously. Fox[10] reported a patient with relapsing meningitis due to Type 29 pneumococci. Elvidge and Roseman[11] used sulfapyridine successfully in treating a patient who had three attacks of meningitis following a skull fracture. Nearly all of the patients reported with multiple attacks of meningitis were adults.

Establishment of the source of infection in the present case has not been possible. Repeated skull films failed to reveal any evident fracture line. Radiographs were taken of all the long bones, but no osteomyelitic process was evident. Mastoid films and radiographs of all sinuses were taken with negative results. A simple mastoidectomy and an adenoidectomy were performed. Methylene blue was instilled intrathecally in an attempt to ascertain the possibility of a crack in the cribriform plate. His serum was assayed for presence of gamma globulin and this was at a normal level. Finally his tonsils were removed. None of the above measures has been of any avail, but the pneumococcal organism responsible for infection has remained sensitive to large doses of penicillin throughout seven recurrent episodes of disease.

SUMMARY

1. A case of seven bouts of pneumococcic meningitis with recovery has been reported.

2. This case demonstrates the fact that one infection with a pneumococcal organism renders no immunity towards a further attack.

3. Penicillin in massive doses is the drug of choice in pneumococcal infection.

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A CASE OF CYCLOPS*

GEO. M. WHITE, M.D., C.M., F.R.C.O.G.,
and THOMAS A. FOSTER, M.D., C.M.,
Saint John, N.B.

MONSTROSITIES are one of the most heartbreaking tragedies of pregnancy, both to the parents and the obstetrician. Congenital anomalies occur in about 1% of births, but the percentage of monsters is much lower than this. It is truly amazing, with the multiplicity of possibilities for embryological development to go astray, that the incidence of anomalies is as low as it is. We would like to present a malformation which has been of considerable interest to embryologists, but is also of general interest, because of its rarity and marked deviation from normal development.

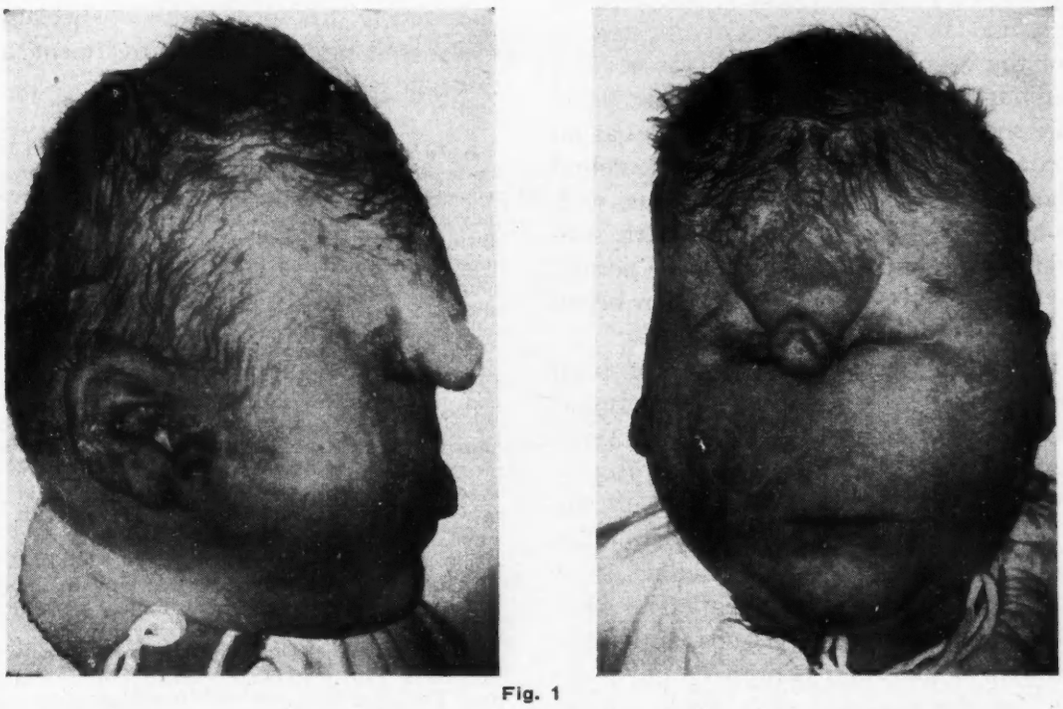

Fig. 1

Mrs. M.B., a 24-year-old gravida iii, was first seen with this pregnancy on September 14, 1953. Her last menstrual period had been June 28, and her due date was approximately April 4, 1954. Her personal and family history were both negative. She had had two full-term pregnancies: one on March 2, 1950, and one on April 2, 1951. Pregnancies, labour and children were all normal.

Her prenatal course during this pregnancy was uneventful. Her temperature, pulse, respirations, blood pressure, urine and weight gain remained normal. Her Wassermann reaction was negative, and she was Rh positive.

On April 2, 1954, her abdomen was radiographed because the enlargement did not correspond with her period of amenorrhœa. The radiologist reported a 7½(?) month fœtus, vertex presenting, and suggested the possibility of microcephaly.

On May 12 the patient started labour spontaneously and, after a short labour, delivered a male child, weighing 7 lb. 8 oz., from an ROA position. The baby was a dead-born monster. The mother's post-partum recovery was normal.

Autopsy was performed on the baby on May 13, 1954, and the report of the pathologist was as follows:

The body weighs 3,300 grams. The head of the infant is grossly abnormal. The nose is absent from its normal site, and from the frontal region sprouts a tubular structure two inches in length with apertures at the tip.

The palpebral fissures are separate, but set more closely together than normal, at a lower level than, and lateral to, the nasal protuberance. There is only one orbit, and no global tissue can be detected. The mouth of the infant is small and the central philtrum is absent from the upper lip. The head is smaller than normal, and this appears to be due to a deficiency of the frontal region.

The rest of the body appears to be grossly normal. The testicles are in the scrotum, and there are no signs of prematurity.

Heart and lungs are obscured by a large thymus gland. The heart appears to be occupying a somewhat transverse position, but there are no other gross abnormalities present in the thorax.

There are no gross abnormalities apparent in the peritoneal cavity.

The heart has many of the characteristics seen in the tetrad of Fallot. There is a large left ventricle communicating with a much smaller right ventricle by a high septal defect (through the membranous part of the septum). The aorta over-rides the septal defect and is a larger vessel than normal. The pulmonary trunk, on the other hand, is small. The atrial septum is complete and there is no defect present. The cardiac musculature is normal and there is no hypertrophy of the right ventricle as seen in a true Fallot tetralogy. There is a ductus arteriosus which admits a small probe. The valves of the heart are normal save that there are only two cusps present in the pulmonary valve.

The lungs are airless but are not abnormal. The air passages are clear of aspirated material.

Liver and biliary apparatus are normal. The spleen, kidneys and genito-urinary system are normal.

*From the Department of Obstetrics and Gynæcology of the Saint John General Hospital, Saint John, N.B.

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The adrenal glands are not present as such, but the elements may be present, though not collected into definite organs. The pancreas and alimentary system appear normal on careful naked-eye examination.

The shape of the head has already been noted. The anterior fontanelle is occupied by a diamond-shaped piece of bone. On incising the dura, amber fluid is noted, and the brain substance is reduced in amount and lies in the middle and posterior fossæ. The condition appears to be a fusion of the cerebral hemispheres, with a failure of the frontal and occipital lobes to develop. The single ventricle herniates through the deficiency and occupies most of the cranial cavity, the lining fusing with the dura over the vault of the skull. The fused cerebrum contains "horns" of the ventricle. The amber fluid comes from the ventricular system. The cerebral convolutions are poorly developed, as are cranial nerves I and II. The aqueduct of Sylvius leads from the base of the single ventricle and may be seen from above through the deficient roof of the ventricle. The mid-brain, cerebellum and medulla appear to be normal.

DISCUSSION

The presence of the superiorly placed nasal proboscis, and the greater or lesser degree of fusion of the central eye, are the most obvious abnormalities in a cyclops. However, the head is usually somewhat small and the brain has an almost constant pattern, in which the cerebral hemispheres are fused into a single mass, with a single open ventricle and the hemispheric substance reduced to one-third or less of the normal volume. Usually the portions of the brain below the cerebral hemispheres are normal.

The failure of facial development has been interpreted in two ways. Firstly, it may represent a secondary fusion of primordia that arise separately, which results from a failure of the frontonasal process to grow downward and of the bones of the nose to develop, thus permitting the eyes to come together in the midline, since nothing is present to keep them apart. The other theory, and probably the correct one, is that the malformation of the brain is primary and is responsible for the existence of a single anlage, which may remain single or may undergo partial division, and that the absence of the bones of the nose is secondary to the abnormal location of the central orbit.

SUMMARY

A case of cyclops is presented with the typical findings of cerebral hemisphere abnormalities, one central orbit, no global tissue, and a misplaced nasal proboscis. The abnormalities in the heart and the probable absence of the adrenals merely lend support to the old dictum "when one congenital abnormality is detected look for others."

PSYCHOSIS FOLLOWING REMOVAL OF A PARATHYROID ADENOMA FOR HYPERPARATHYROIDISM*

MICHAEL KAYE, M.B., B.S.,
COOPER H. STACEY, M.D. and
ISADORE ROSENFELD, M.D., *Montreal*

EMOTIONAL CHANGES have frequently been observed in association with hypocalcæmia due to parathyroid insufficiency. Occasionally, psychoses occur.[1, 2] Cases of this type due to idiopathic hypoparathyroidism,[3, 4] and following thyroidectomy with damage to the parathyroids, have been described.[5, 6] Occasionally after removal of a parathyroid adenoma for hyperparathyroidism, a psychotic state associated with hypocalcæmia and tetany has occurred.[1, 7, 8] Because of its rarity, and the response to treatment, a case of this type is reported.

A 49-year-old white woman was admitted to hospital on September 21, 1952. Her complaints were anorexia, epigastric discomfort, nausea, vomiting, constipation, polyuria and polydipsia for one year, 40 lb. weight loss during this period and pains in the long bones for six months. Memory impairment with, at times, difficulty in thinking clearly, blurred vision and generalized weakness had been present for five years. She described herself as always "nervous".

The past history revealed that in 1937 she had been admitted to the Royal Victoria Hospital for dysuria, right loin pain and fever. The history taken at that time stated that she had experienced attacks of these symptoms for many years, and had passed a calculus one year previously. In addition dyspepsia, constipation and some weight loss was noted. Renal investigation at that time revealed an early right hydronephrosis with a double right ureter. No calculus was present. She was discharged on symptomatic treatment. In 1942 she was admitted to another hospital for similar symptoms. In the family history, all four siblings were reported as being nervous.

Examination at the time of her present admission showed a rather anxious woman with evident weight loss. The skin was dry. No swellings were felt in the neck, and the extremities, heart and lungs were normal. The blood pressure was 160/85. Costolumbar tenderness was present bilaterally, and the lower pole of the right kidney was palpable. The liver edge was felt 5 cm. below the right costal margin, but the spleen was not palpable. The bones were tender to pressure and the deep tendon reflexes were all brisk. The remainder of the examination was normal.

The laboratory findings were as follows: Hæmoglobin 11.7 gm. %, red cell count 3,920,000. Examination of the urine showed a specific gravity of 1.010: no albumin or sugar. There were 10-15 white blood cells per high power field in an uncentrifuged specimen. The Sulkowitch test was strongly positive. Phenolsulfonephthalein test showed 45% excretion in 2 hours. Gastric analysis did not reveal any free acid after histamine. The blood sugar was 95 mgm. % fasting and 116 mgm. % after food. Non-protein nitrogen 27.5 mgm. %. Total serum

*From the Department of Medicine, and the Allan Memorial Institute of Psychiatry, Royal Victoria Hospital, Montreal.

proteins 6.96 gm. %, albumin 4.4 gm. %, globulin 2.56 gm. %. The serum calcium was markedly elevated, varying between 16.7 mgm. % and 17.2 mgm. %, inorganic phosphorus 2.54 mgm. %. The alkaline phosphatase was 47 King Armstrong units, acid phosphatase 3.7 units. The Kahn reaction was negative and the basal metabolic rate plus 10%.

Liver biopsy showed normal tissue. Radiographs of the skull and long bones were normal, and did not show any evidence of osteoporosis or osteitis fibrosa cystica. Examination of the gastrointestinal tract with barium swallow, meal and enema was also negative. Following intravenous pyelography no satisfactory excretion of dye was obtained, but bilateral nephrocalcinosis was noted. Cystoscopic and retrograde pyelography revealed a right bifid pelvis and ureter with hydronephrosis, and a small renal calculus on the same side.

The patient's behaviour was one of moderate apprehension, but she was co-operative, although somewhat disturbed by the various diagnostic procedures.

Dihydrotachysterol (A.T. 10) 1 c.c. twice daily was started on Oct. 26 and increased to 2.5 c.c. twice daily on Oct. 29 and 3 c.c. twice daily on November 5. 50,000 units of vitamin D were given daily from October 28 to November 12. Additional treatment consisted of calcium gluconate 2 gm. intravenously daily and 10-12 gm. orally, a low phosphorus diet and aluminum carbonate gel (basaljel) 8 c.c. twice daily. The effect on the calcium levels can be seen from Fig. 1. Sedation was with methyl parafynol (Dormisone), 0.75 gm. once or twice daily, and chloral hydrate gr. 20 at bedtime. No other therapy was given.

At the time of transfer, her psychiatric state clinically was that of an agitated depression, with increased psychomotor activity, numerous somatic complaints and marked anxiety requiring constant reassurance. Affect was depressed, sensorium clear and orientation correct. No hallucinations or delusions. Physical examination was essentially unchanged except for pitting œdema of the ankles, first noted on October 20, and desquamating skin on the extremities, residuum from the previous erythema.

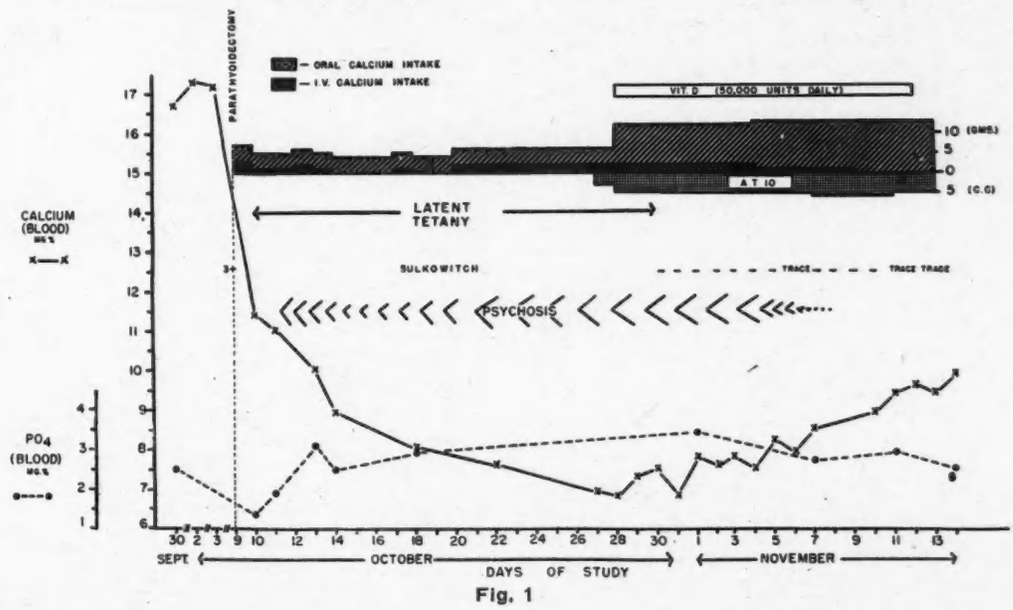

Fig. 1

On October 9, 1952, a parathyroid adenoma 1.2 cm. in diameter was removed from the left side of the neck, beneath the upper border of the sternum. Three normal parathyroid glands were identified. One of these became detached during dissection and was reimplanted. The operative and immediate postoperative course was uneventful. The serum calcium and phosphorus can be followed from Fig. 1. Additional calcium was given as indicated, initially 4 gm. of calcium gluconate orally, and 10 c.c. 10% calcium gluconate intravenously once or twice daily. Tetanic symptoms commenced on Oct. 10, consisting of numbness and tingling in the fingers and toes, with tightness of the face and throat. Chvostek's sign, which had not been present earlier, was elicited from Oct. 27, but Trousseau's sign remained negative.

On Oct. 12, mental symptoms became prominent. She became increasingly anxious and depressed, requiring frequent reassurance. She described bright lights into which she was being drawn, also a fear of sinking into a hole. She believed her mind was racing and felt she was going to die. Intravenous calcium gluconate had no immediate effect on the mental state. Sedation with phenobarbital gr. 2 every 6 hours and seconal gr. 3 at bedtime, was started on Oct. 13, but discontinued on Oct. 19 because of the development of a generalized itchy rash. A temporary improvement occurred in the mental state when she was receiving sedatives, but from Oct. 19, anxiety, agitation, and depression became more marked. On Oct. 27 she was transferred to the psychiatric service.

Psychological testing was carried out on October 30, using the abbreviated Wechsler Bellevue (VIBS), Wechsler Memory Scale, and Bender Gestalt tests. The former showed an I.Q. of 84 with a memory quotient of 67. The summary indicated an extremely agitated insecure woman with dull normal intellectual capacity. Behaviour and signs of weakened reality contact suggested a psychotic condition, with agitation and depression as the outstanding features. The Rorschach and Figure Drawings on November 3 showed confused, illogical, autistic thinking, giving evidence of a psychotic state. Some features indicating organic involvement were present.

Electro-encephalogram was normal on October 30 when the serum calcium was 7.5 mgm. %, with a well-regulated 8½-9 c.p.s. occipital alpha rhythm.

The patient remained restless, apprehensive and depressed until November 3, from which date slow but steady improvement was noted. This coincided with the gradual rise in her serum calcium level. Plasma proteins remained unchanged at 6.85. gm. %. Albumin 4.78 gm. % on October 22, and 6.36 gm. % on November 5. The alkaline phosphatase fell to 43.7 units on October 28, 33.6 units on November 3 and 24.4 units on November 14. She began to gain weight, eat and sleep well, appeared more cheerful and mixed with other patients. No sedatives were required during the day. At the time of discharge on November 14, 1952, her confusion and

agitation had disappeared, leaving only a moderate degree of anxiety. Treatment to take at home comprised 2 c.c. of A.T. 10 twice daily and 14 gm. calcium gluconate orally daily, with an ordinary diet.

The patient was seen again on December 16, 1952. Weekly determinations of the serum calcium subsequent to leaving hospital had varied between 9.0 and 11.4 mgm. %. The doses of A.T. 10 had been gradually reduced to 1 c.c. twice daily and additional calcium to 6 gm. of calcium gluconate daily. She had gained 10 lb. in weight, and was able to carry on her usual household duties. On questioning, she stated that her nerves were better than before the operation and that she felt well. She appeared slightly anxious, but there was no evidence of the previous agitation or depression.

All the psychological tests were repeated, alternate forms being given in the two Wechsler tests. Intellectual functioning did not improve significantly (I.Q.89), but there was a marked improvement in the memory scale, particularly in her ability to concentrate, assimilate new learning, and recall perceptual stimuli. The M.Q. had risen from 67 to 93. Definite changes were present in the Bender Gestalt test, with disappearance of psychotic signs, and these together with the results of the memory scale indicated a decrease in organic factors. The Rorschach and Figure Drawings showed less confusion, better motivation and greater social awareness, but continued evidence of poor ego control indicated that underlying psychotic features were still present. The conclusion was that noticeable changes for the better had occurred, and these would probably continue, but it was suspected that her adjustment would always be poor under stress-producing circumstances.

The patient was last seen on April 7, 1953. A.T. 10 had been discontinued on January 7 and additional oral calcium was stopped on January 21. Her satisfactory progress had been well maintained, and the serum calcium level had remained between 9.6 mgm. and 11.0 mgm. %.

DISCUSSION

The importance of the calcium ion in the regulation of the excitability of nervous tissue is well-known.[9] A sudden marked change in the ionic level is less well tolerated by the body than a more gradual one. While an acute change, as in this case, may produce florid symptoms, in chronic hypocalcæmia the disturbance in mental and physical functioning is often less marked.[10]

Psychiatric symptoms in hypocalcæmic tetanic states may be of any type. Anxiety is frequent in all, but any combination may occur, of which the following are the most frequent in the cases reported previously: depression, agitation, confusion, suicidal thoughts, hallucinations, delusions, and ideas of reference.[1, 2] In every case, improvement, which is usually permanent, is noted following maintenance of normal calcium levels.

The importance of instituting adequate substitution therapy when a parathyroid adenoma is removed, is stressed. In those cases with a high alkaline phosphatase the danger of tetany postoperatively is greatest, and treatment is best started immediately prior to operation.[11] In all, the importance of intensive treatment as soon as any signs of tetany or emotional changes occur following operation is apparent, for thereby the possibility of a serious psychotic breakdown may be prevented.

Although some mental symptoms following this operation are not uncommon, the extremely rare occurrence of psychosis is of interest. Probably this is partly due to prompt substitution therapy when tetanic symptoms occur, but in addition the previous personality must be of considerable importance.[7] This is exemplified in this patient. She had always tended to be "nervous" and the psychological tests suggested that her personality pattern was poorly constructed to meet stress-producing situations.

SUMMARY

A case is reported of primary hyperparathyroidism, with postoperative hypocalcæmia and tetany. This was associated with an acute psychotic breakdown, the clinical condition being that of an agitated depression. Following a low phosphorus diet, additional calcium, vitamin D and A.T. 10, the calcium levels returned to normal. Concomitantly, improvement in the mental state occurred.

We wish to thank especially Dr. M. Aronovitch, under whose care the patient was, for permission to publish this report, and also all those who have contributed to this paper by their interest in the patient and advice regarding her management.

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THE GRACE OF GOD

No hospital can rise higher than its medical staff; and medicine will remain a profession just as long as physicians are gentlemen before they are business men and scientists. For medical practice is science tempered with emotion and sympathy. Similarly hospitals will remain hospitals just so long as they practice courtesy. For in courtesy is the grace of God.—(E. P. Scarlett, *Canad. Hosp.*, 31: 33, Dec., 1954.)

BRUCELLOSIS AND MILIARY TUBERCULOSIS IN AN ESKIMO WOMAN

CAMERON CORRIGAN, B.Sc., M.D. and SAMUEL HANSON, M.D., *Edmonton, Alta.*

WHILE THE FINDING of brucellosis and tuberculosis in the same individual is not unknown, we feel it is rare enough to warrant recording a case—particularly when the patient is an Eskimo who spent her entire life at Bathurst Inlet in the Canadian Arctic.

On the night of May 10, 1954, a 49-year-old Eskimo woman from Bathurst Inlet was admitted to the Charles Camsell Indian Hospital with a history of frequent nose bleeds and loss of weight. Because of language difficulties no history was obtained from the patient herself. She was an extremely ill emaciated old woman who was very dyspnœic and obviously very anæmic. Physical examination revealed no abnormality of the head and neck. The patient had a rapid pulse (110) with some shift of the cardiac apex to the left. There was a systolic murmur at the apex which extended into the axilla. B.P. was 96/50. There were numerous crepitations at both bases. Examination of the abdomen revealed an enlarged and tender liver. No ascites was noted. Examination of the lower limbs revealed moderate pitting œdema of the ankles. Temperature was 103° F., pulse 110, respiration rate 30. A chest radiograph on admission was read as showing bronchopneumonia with superadded congestive heart failure. However, repeat radiography was advised in order to rule out an underlying miliary tuberculosis. An admission diagnosis of congestive heart failure with bronchopneumonia was made. The patient was digitalized and penicillin ordered. On May 11, laboratory findings were: white cell count 2,850 per c.mm., red cell count 2,400,000 per c.mm.; Hb value 5.5 gm. %; sedimentation rate 125 mm. in one hour. In view of the blood picture a Widal test was ordered which showed Brucella agglutination at 1/100. On May 12 it was felt that the patient was somewhat improved. The œdema of the ankles disappeared and the liver decreased in size. However, the temperature continued to swing between 100 and 103° F.

On May 13, a sternal puncture was performed. Study of bone marrow smear failed to reveal any blood dyscrasia. The marrow was cultured and at the time some marrow was embedded and processed for histological study.

On May 12 and again on May 13 the patient received a blood transfusion of 500 c.c. On May 11 to 13 direct smear examinations of the sputum were negative for acid-fast bacilli. On May 14, histological examination of the embedded bone marrow revealed granulomatous foci, and a diagnosis of miliary tuberculosis was made. Antituberculous treatment with one gram of streptomycin and 250 mgm. of isoniazid and PAS daily was instituted. On May 15, special stains re-

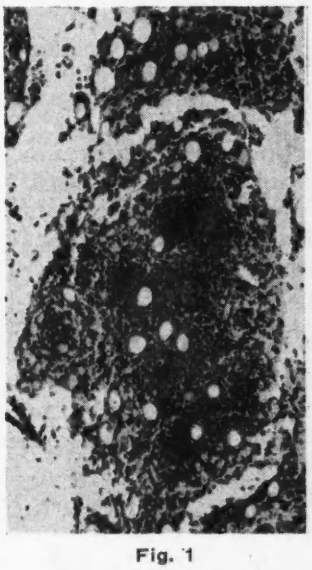

Fig. 1

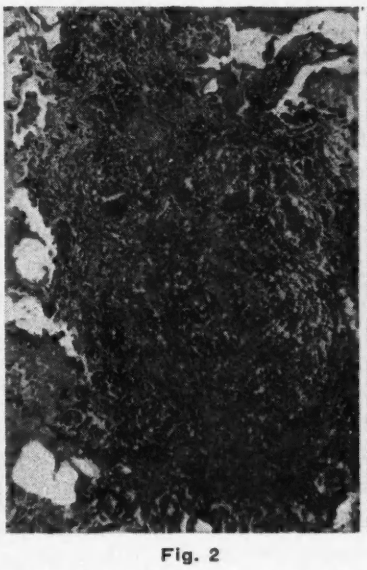

Fig. 2

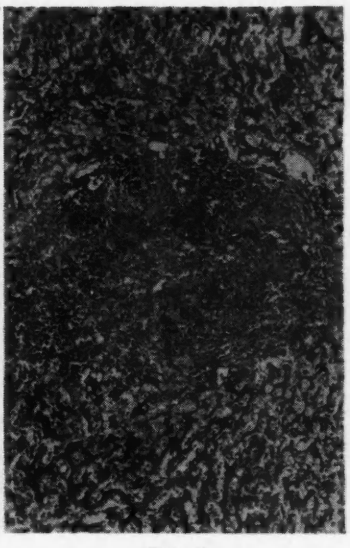

Fig. 3

Fig. 1.—Chronic granulomatous focus in bone marrow. Fig. 2.—Chronic granulomatous focus in lung. Fig. 3.—Chronic granulomatous focus in liver.

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vealed AFB in the embedded sternal marrow, and direct smear examination of the sputum revealed AFB.

On May 15, the temperature became normal for the first time since admission. Over a period from May 11 to May 22 the patient received five blood transfusions. On May 26, it was felt that her condition was deteriorating. She became weaker. Œdema of the hands and feet developed and ascites was present. She died rather suddenly on May 28. On June 8, a report from the Provincial Bacteriology Laboratory reported isolation of an organism of the genus Brucella from the sternal marrow submitted on May 13 and cultured on liver agar slant.

A pathologist's report follows:

The principal pathological findings, before death, resulted from study of the bone marrow. Sections of bone marrow particles stained with hæmatoxylin and eosin revealed the presence of granulomatous foci (Fig. 1). These foci were composed of collections of epithelioid cells, plasma cells, neutrophils and lymphocytes with the occasional Langhans type of giant cell. Kinyoun stains of this bone marrow revealed acid-fast bacilli present in these granulomatous foci. Fluorescent microscopy studies were positive for *Myco. tuberculosis.*

Culture of this bone marrow employing liver agar slants with liver infusion broth yielded a pure growth of an organism of the genus Brucella.*

Postmortem findings.—An autopsy was performed 36 hours after death. The principal finding was multiple granulomatous foci in the lungs, liver, spleen, lymph nodes and kidneys (Figs. 2 and 3). Culture of the bone marrow and guinea-pig inoculation of bone marrow yielded *Myco. tuberculosis.* Acid-fast stain and cultures from the organs also revealed *Myco. tuberculosis.* Cultures of autopsy material for Brucella were all negative.

SUMMARY

A case of miliary tuberculosis and brucellosis in an Eskimo woman is reported.

This definitely establishes the fact that brucellosis exists in the Canadian Arctic. The vector is not known but is likely to be caribou.

*These studies were carried out at the Provincial Laboratory of Public Health, University of Alberta, and are to be the subject of a future report by them.

Clinical and Laboratory Notes

OXIDIZED CELLULOSE (GELFOAM) AS A HÆMOSTATIC FACTOR IN GENERAL SURGERY

E. KONSECK, M.D., *Regina, Sask.*

OF THE HÆMOSTATIC AGENTS applied during the past decade (thrombin, fibrin foam, oxidized cellulose) the gelatin sponge has, in our experience, proved to be the most suitable. The sponge is applicable in all fields of surgery, such as thoracic surgery, neurosurgery, abdominal surgery, gynæcology, urology and ENT surgery, and also in dental treatment (Defoort, Brussatis, Bing), especially where, due to small and not easily accessible bleeding points, control of bleeding is rendered more difficult. By virtue of its various other characteristics it has also been applied in fields other than the control of bleeding.

Gelatin sponge (Gelfoam) consists of sterile gelatin solution which is hardened, dried and rendered porous by means of air. It is manufactured in sections 1 cm. thick and may easily be cut into pieces of various sizes. By saturation with physiological saline solution it may easily be shaped and is thus readily adaptable to any surface. A piece which just covers the bleeding surface is cut, saturated with physiological saline solution, squeezed to remove air bubbles and then held in place with moderate pressure for approximately one to two minutes, until it clings firmly to the surface. For more effective control of bleeding the sponge is saturated with thrombin (500-1,000 units per c.c.). The sponge has also been found useful as a vehicle for various drugs, such as penicillin.

When the sponge is applied in aseptic cavities, these may be closed immediately and the sponge left in the cavity, since it is liquefied and does not cause any tissue reaction. In the case of septic cavities the sponge is first saturated with a solution of an antibiotic.

The effect is partly mechanical, i.e. the sponge, which is saturated with blood (it can absorb 45 times its weight in whole blood), acts as a tampon by pressure. Its controlling effect in bleeding is caused by clotting.

In open cavities, e.g. after removal of the gallbladder and in rupture of the liver or kidneys, especially after bullet wounds, the following process may be observed. The gelatin sponge is liquefied after some days on the side facing the bleeding point. Protected by the liquid layer of gelatin, the underlying tissue begins to granulate and epithelialize, and quick

restitution takes place. This is not delayed by the application of antibiotics. The larger part of the sponge is then automatically discharged. In non-infected tissue there is close contact between tissue and sponge by means of connective tissue and blood elements, until the sponge is completely absorbed.

In cases of epistaxis the surgeon endeavours to control bleeding immediately. Tamponade by means of iodoform gauze or otherwise used to be employed; either a front one is performed or a rear one towards the epipharynx, in which case the tamponade itself is very painful; the whole nose is blocked, and headache may occur. This method invariably causes the mucous membrane to suffer, so that when the tampon is removed not only is the original bleeding point affected, but there are also several new bleeding points. For these reasons this kind of tamponade may possibly disappear and be replaced by application of Gelfoam sponge.

Histological examination of rabbits (Bing, Pellegrini) shows that in sterile wounds after eight days the sponge has become agglutinated with its surroundings through a network of connective tissue. Fifteen days after application the sponge is considerably smaller; a connecting layer has now formed between sponge and tissue which consists of fibrocytes, fibroblasts and proliferated small vessels, which advance towards the interior of the sponge. Macroscopically, there is nothing to be seen of the sponge after a period of 35 days, except when the quantity used has been excessive. Histologically there is only fine scar tissue to be seen. Histological examination and clinical experience have shown that the gelatin sponge is excellently responded to by the tissues, a factor which opens up further fields of application for Gelfoam.

Generally it may be used for the control of any kind of bleeding, whether the bleeding is parenchymatous or originates from a small vessel. In the latter case a correspondingly large piece of gelatin is pressed on to the vessel for one or two minutes. The sponge will then cling to the wall of the vessel and will control the bleeding. Should, for instance, ligature be impossible, control of bleeding by tamponade with Gelfoam may suffice.

In some kinds of bleeding, such as that due to hæmorrhagic diathesis, or thrombopenias, or toxic bleeding of the mucous membrane after infectious diseases or in chronic leukæmia, when the whole surface of the mucous membrane either bleeds or is excessively vulnerable, Gelfoam has proved to be most suitable. When controlling bleeding caused by hæmorrhagic diathesis or thrombopenias, the bleeding surface should be covered with the Gelfoam sponge, which is held in place for three to four minutes (depending on the extent of the field of bleeding), until the side of the sponge facing the bleeding point firmly clings to the latter.

Instead of saturating the Gelfoam sponge with physiological saline solution, thrombin solution may be chosen, in order to control bleeding better. If the bleeding points are not directly visible, a piece of Gelfoam is applied to the area of bleeding in the way mentioned above. Gelfoam has also been used successfully after nose operations such as removal of polyps or mucotomy. In the treatment of patients with a predisposition to bleeding, the Gelfoam tamponade is the only solution to the problem. Tamponade with Gelfoam is highly recommended for ambulant patients who live a considerable distance from hospital.

In aural surgery the sponge is used for tamponade of the auditory meatus. The sponge is saturated with penicillin, then placed in the radical mastoid operation cavity, where it is left for five to seven days. During this period penicillin is frequently added to the sponge in order that granulation may be prevented. It is of special advantage that a torn lobe of the tympanum is agglutinated again, that the Thiersch lobe, because of moderate tampon pressure, clings more firmly to its base, and that there is faster agglutination with the surrounding tissue. To support this process, the base is wet with a thrombin-plasma spray, and the sponge may easily be removed without residue. The surface of the sponge is capable of absorbing large quantities of fluid and thus keeps the radical operation cavity dry. Bleeding from nutrient vessels or dura may also be checked with Gelfoam during operations.

During the past year approximately 4,000 general surgical cases were operated on in Grey Nuns' Hospital, Regina; in about 8% of these cases the use of Gelfoam was indicated. There were no postmortem examinations of patients treated with Gelfoam during operation.

SUMMARY

Gelfoam tamponade has, in almost all fields of medicine, particularly in surgery, become the most favoured method of control of bleeding because it is easy to apply and painless. It is more economical and more exact than any other tamponade known.

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THE BACTERIAL FLORA OF THE URETHRA IN NON-SPECIFIC URETHRITIS

R. R. WILLCOX, M.D.,*
London, Eng.

MANY WORKERS have discussed the large number of possible causes of non-specific urethritis.[1, 3, 4] When the more definite entities have been excluded, the majority of cases remaining have been classified as "bacterial urethritis" and "abacterial urethritis," according to whether or not bacteria have been observed in the smear.

Ordinary cultures from the urethra in non-specific urethritis yield predominantly the urethral *Staphylococcus albus* which has been shown to be largely resistant to neoarsphenamine and sulphadiazine.[2] As the first of these drugs has no action and the second only a variable action in clinical non-specific urethritis, it was considered worthwhile to investigate again the urethral flora of patients with non-specific urethritis before and after treatment with the more effective orally administered antibiotics, and of controls.

Urethral cultures on blood agar were therefore made in 150 instances before and after treatment for non-specific urethritis, and a further 151 cultures were made on controls. All of the patients concerned were attending the venereal diseases department at King Edward VII Hospital, Windsor, England. No attempt was made to differentiate between different types of urethritis other than to exclude the gonococcus by smear examination.

CONTROL CULTURES

These were made on 105 patients of whom 45 were previous syphilitics, 17 had anxiety states, 16 had non-syphilitic genital lesions, 15 had gonorrhœa, eight were attending for routine serum tests and four had non-syphilitic lesions elsewhere on the body. After an interval of one week—longer in a few cases—a second culture was performed on 46 cases. The results are shown in Table I.

TABLE I.

URETHRAL CULTURES FROM CONTROLS

Organism	*First culture (105 cultures)*		*Second culture (46 cultures)*	
	No.	*%*	*No.*	*%*
Staph. albus	72	68.6	30	65.2
Bact. coli	22	21.0	11	23.9
Diphtheroids	19	18.1	9	19.6
Saprophytes	8	7.6	3	6.5
Staph. aureus	4	3.8	—	—
Monilia	3	2.8	1	2.2
Nil	2	1.9	1	2.2

Thus, apart from the absence of *Staph. aureus* in the second test, the results show considerable agreement.

CULTURES FROM CASES OF NON-SPECIFIC URETHRITIS

Urethral cultures were made before treatment on 81 cases of non-specific urethritis and a second culture was taken from 69 patients, usually about a week later, following treatment with either chloramphenicol, aureomycin or terramycin, administered orally (Table II).

TABLE II.

URETHRAL CULTURES FROM NON-SPECIFIC URETHRITIS PATIENTS

Organism	*Before treatment (81 cultures)*		*After treatment (69 cultures)*	
	Cases	*%*	*Cases*	*%*
Staph. albus	66	81.4	55	79.7
Diphtheroids	26	32.1	27	39.1
Coliforms	16	19.7	9	13.0
Saprophytes	4	4.9	9	13.0
Enterococci	2	2.5	—	—
Streptococcus	1	1.2	2	2.9
Staph. aureus	1	1.2	—	—
Monilia	1	1.2	1	1.4
Proteus	—	—	1	1.4

There were thus no very striking differences in the urethral flora of patients with non-specific urethritis before and after treatment with the orally administered antibiotics, or between the cultures from patients with non-specific urethritis before treatment and those from controls.

SUMMARY AND CONCLUSIONS

1. In a study of 301 urethral cultures no significant differences were noted in the bacterial flora of patients with non-specific urethritis and of controls.

2. There were also no significant changes in the urethral flora of patients with non-specific urethritis following treatment with the orally administered antibiotics, a form of treatment which was usually clinically successful, or in repeated cultures in controls without such treatment.

3. It is not considered, therefore, that the organisms noted were the cause of the urethritis, and the condition of "bacterial urethritis" cannot be considered as a common entity until the cause of "abacterial urethritis" has been firmly established.

The cultures were made at the Windsor Group Pathological Laboratory by Dr. E. Sayle, to whom grateful acknowledgements are expressed.

This paper is part of the Report rendered to the British Medical Association at the termination of the Insole Research Scholarship, 1951-52.

*St. Mary's Hospital, London, W.2.

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TREATMENT OF CHRONIC GONORRHŒA WITH LONG-ACTING PENICILLIN

K. G. CAMBON, M.D. and
E. N. CAMBON, M.D.,
Mackenzie, British Guiana

THIS ARTICLE deals with the problem of chronic gonorrhœa in British Guiana. No accurate estimate of its incidence is available but it is believed to be very high.

This study was made in a large bauxite and milling centre in the interior of the country; since most of the subjects were Company employees it was possible to follow up sucessfully most of the treated cases. However, the general attitude to such matters as promiscuity and illegitimacy constantly impedes control measures. This is illustrated by the fact that of 449 children born in the Company Hospital in 1951 and 1952, 198 (44%) were born out of wedlock. This is not a matter which involves any measure of social stigma, society and cultural life in the country having developed standards recognizing it.

Due to inadequate early treatment and constant reinfection, chronic prostatitis and pelvic inflammatory disease are widespread. These respond poorly, if at all, to ordinary penicillin therapy and provide a vast reservoir of infection that nullifies attempted control measures. Moreover, the disease in its chronic form is a real drain on the general health of the community. In males the complaints are of low back pain (described locally as "weariness in the back"), persistent urethral discharge with slight burning on urination, and impotence. On examination, the prostate is found to be moderately enlarged and tender on palpation, and a smear test is positive for gonococci. The pain in the back is sometimes disabling and often ascribed to some injury sustained in the distant past. It can usually be differentiated from actual injury to the back or herniated disc, as there is no limitation of movement of the back and no tenderness, and the leg-raising test can be carried out with ease. In women, the findings are those of chronic pelvic inflammatory disease.

In an endeavour to find a better treatment, an unselected group was treated with the recently introduced long-acting penicillin N:N'-dibenzylethylenediamine dipenicillin G.* A comparable unselected group was treated with procaine and crystalline penicillin G. Smears were taken before and after treatment. No facilities were available for cultures. All were cases of chronic gonorrhœa and all had positive smears before treatment.

The first group received Duapen 600,000 units every four days for a total of 2,400,000 units. Of the 57 patients in the group, seven either did not complete treatment or did not return for re-examination, leaving 50 cases in the study. In this group, the cure rate as judged by a negative smear was 76% (see Table I). The second group consisted of 50 cases taken at random from our records. All this group received procaine and crystalline penicillin 400,000 units daily for five days or a total of 2,000,000 units. Cure rate as judged by a negative smear was 34%.

TABLE I.

	Males	*Females*	*Total*	*After treatment*		
				No symptoms	*Improved*	*No better or worse*
Duapen group:						
Negative smears	30	8	38	28	7	3
Positive smears	8	4	12	4	5	3
Procaine-penicillin group:						
Negative smears	10	7	17	13	2	2
Positive smears	21	12	33	10	12	11

The above results would seem to indicate that Duapen is more effective than procaine penicillin in chronic gonorrhœa. Furthermore, of the ones who resisted treatment, several were given massive doses of Duapen or penicillin without further changing their symptoms or changing their positive smears. One is left with the impression that there is a penicillin-resistant strain of gonococcus. However, there are no facilities available at the moment to test this bacteriologically.

I am indebted to the Demerara Bauxite Company, Limited, for permission to publish this article.

**Duapen*, Ayerst, McKenna & Harrison Limited.

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(Information regarding contributions and advertising will be found on the second page following the reading material.)

Editorials

FLUORIDATION AT BRANTFORD

The Brantford study of the effects of artificial fluoridation of local water supplies goes its expected way. The 1954 report, published in the *Journal of the Canadian Dental Association* (20: 585, November 1954), shows that, after nine years of fluoridation of the Brantford, Ontario, water supply to one part of fluoride per million, the effect on dental caries reduction has been very much that predictable while no harm to the populace has been detected. For those who have not followed the study closely, it should be explained that three localities are involved in it: (1) Stratford, whose inhabitants drink water with a natural high-fluoride content; (2) Brantford, whose inhabitants used to drink almost fluoride-free water up to 1945, and who therefore had a much higher caries rate than their Stratford neighbours; since 1945, Brantford has artificially remedied its fluoride deficiency; (3) Sarnia, whose inhabitants continue to drink low-fluoride water. Since 1945, the caries rate in Brantford children has declined each year, while that in Sarnia children has remained steady. The proportion of Brantford children aged six to eight years (and therefore never exposed to fluoride-free water) with caries-free permanent teeth is now about twice as great as for Sarnia, and the mean DMF (decayed + missing + filled) tooth rate in this age group in Brantford is less than one-quarter of the Sarnia rate. As might be expected, improvement in caries rates in older children was not so obvious, since these youngsters had started their enamel formation on fluoride-free water. Another point made in the latest report is that the six to eight-year-olds in Brantford have now a caries rate comparable to that of their Stratford counterparts drinking naturally fluoridated water.

No Brantford medical practitioner has observed any ill-effects which might have been attributed to artificial fluoridation. One curious finding is that, although careful examination revealed slight mottling of teeth in certain Brantford children – an effect usually attributed to fluoride – similar mottling was also occasionally found in fluoride-free Sarnia. Since the amount of mottling was negligible, the finding is of no practical significance.

Editorial Comments

INTRAMUSCULAR IRON THERAPY

The injection of iron as a form of therapy has undergone some vicissitudes in the last few decades. Twenty years ago, a noted English clinician used to tell his students that "the man who treats anæmia by injecting iron is either a rogue or, what is worse, a fool." Nevertheless there were patients with iron-deficiency anæmia who for some reason or another (failure of absorption or storage) failed to respond to oral administration of iron. Nissim's announcement in 1947 of successful treatment of iron deficiency anæmia by intravenous injection of saccharated iron oxide was therefore welcome. The drawbacks of this procedure have gradually become apparent, for toxic reactions due to allergy or to intravascular precipitation of iron have been recorded and though rare may be serious.

The intramuscular injection of iron has been practised for a long time, but has had the disadvantages of uncertainty of action and causation of severe local pain. Three sets of observers in the United Kingdom have now reported successful trials of a dextran-iron preparation (Imferon) containing 5% iron for intramuscular use. The first paper[1] on this product was published on November 6 and written by Baird and Podmore of Sheffield. They reported that the product causes no more discomfort on injection than such drugs as penicillin. It is true that it causes temporary staining of the skin, but this is of little significance if the gluteal area is chosen, a 2½ inch needle used, and a Z-shaped track made on insertion of the needle. The other two sets of observers, Cappell *et al.*[2] and Scott and Govan[3] (both from Glasgow), whose publications closely followed that of Baird and Podmore, also observed staining. Cappell *et al.* discuss this minor drawback which they claim to have prevented

by injecting 1-2 ml. of air after the solution. In the two cases treated before they had devised this simple method of prevention, pigmentation appeared within 24 hours and was still obvious four months after the injection. Biopsy showed that the staining was due to iron pigment in phagocytes together with an increase in melanin.

None of the authors observed either local or general reactions after the injections, though one mentions at second hand the appearance of an urticarial rash.

Altogether 105 cases of iron-deficiency anæmia were treated, of which 50 treated by Scott and Govan were in pregnant women. Absorption of iron was good; in one series, serum iron levels of up to 2,860 micrograms per 100 ml. were encountered within 18 hours, and absorption via lymphatics was demonstrated histologically. The high serum level did not lead to reactions. Utilization was also good, hæmoglobin increase being on an average 0.3-0.34 gm. for every 100 mgm. injected, and weekly regeneration rates for hæmoglobin of 3.5-11.3% being attained in the first month of treatment. Some of the patients had been either refractory to, or intolerant of, iron by mouth. All patients, with two exceptions (one in uræmia, one with bronchogenic carcinoma), responded, though response was sometimes delayed.

As might be expected, no optimum schedule of dosage has as yet been laid down but in general a dose of 5 ml. of the preparation (250 mgm. iron) twice a week appears convenient and adequate for out-patients, though one group gives 200 mgm. iron every other day, and in-patients may be given the whole dose of iron necessary in three or four days. Many cases of mild anæmia required only two 5 ml. ampoules (500 mgm.).

The indications for the use of this new preparation are, of course, the same as those for intravenous injection of iron, namely, intolerance to or lack of response to oral iron.

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2. *Brit. M. J.*, **2**: 1255, 1954.
3. *Brit. M. J.*, **2**: 1257, 1954.

THE MEDICAL ILLUSTRATORS DIRECTORY

We have received a copy of the 1954 membership directory of the Association of Medical Illustrators. The art of illustrating medical subjects is an old one, dating back to the earliest period of medical teaching, but with many vicissitudes of repression. Some of the great artists have left us anatomical drawings and paintings—Leonardo da Vinci, Dürer, Rembrandt, Rubens. That these were artists first and anatomists second has only heightened the technical value of these particular drawings. Who reads (or has read!) Vesalius for his anatomical descriptions? But who does not know the entrancing woodcuts with which van Kalcar, Titian's pupil, has made Vesalius' work immortal?

Nowadays we may not have academicians doing medical illustrations (though there is no reason why they shouldn't), but we do have artists who are thoroughly trained in this peculiarly exacting art. That is why the quality of our modern medical illustrating is so high.

This Directory tells us who our medical illustrators are on this continent and in Great Britain and what they have done. May it encourage writers in medical and other scientific fields to turn to them for constant guidance in preparing their illustrations. The Directory is to be obtained from the Medical Art Department of the Massachusetts General Hospital, Boston 14, Mass.; the price is one dollar.

B.P.C. 1954

The fact that a new edition of the British Pharmaceutical Codex[1] is needed only five years after the last, in spite of the issue of a supplement in 1952, reflects the rapid advance of pharmacology. Earlier editions came out at intervals of 11 to 15 years without much protest from the users, but a 15-year-old Codex would not be of much value to anyone now. The more realistic approach to drug treatment is also reflected in the orgy of deletions of preparations no longer considered important. This slaughter of the innocents—and impotents—has involved some old favourites such as guaiacol, hydrastis, oil of sandalwood, and even the good old brimstone and treacle (confectio sennæ et sulphuris), as well as some preparations such as oleum neroli, lonchocarpus, kaladana and holarrhena, whose existence must have been known only to the most erudite.

Nobody will feel robbed by these deletions when the impressive list of additions is taken into consideration. Some are really newcomers to medicine—antibiotics, anticoagulants, hypotensives, diagnostic agents and antimalarials—but surprisingly enough some turn out to be old acquaintances made respectable by their inclusion in this, the standard reference work for British pharmacists. Thus the colocynth and hyoscyamus pill discarded by the B.P. is now taken up by its adjuvant, the B.P.C.; glycerin of borax, mercury with chalk and liniment of belladonna are among the many which have made this journey from one book to the other.

Some preparations have changed their name, though in many cases the change is trivial (sulphated castor oil for sulphonated castor oil, bismuth sodium tartrate for sodium bismuthyl tartrate), and in others of debatable value, as in the change of trichloracetic acid to trichloroacetic acid and anti-venom serum to venom antiserum.

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A most welcome part of the new Codex is the loose supplement which gives a list of proprietary synonyms for official names and vice versa. Such is the present state of therapeutics that many are incapable of navigation in the sea of unfamiliar B.P.C. names without this chart.

Perhaps it is impertinent to praise or to criticise this work; if praise may be permitted, we would commend the masterly summaries of "actions and uses" of drugs. They are models of compression and clarity. As to criticism, there still seem to be a few candidates for the axe lurking in corners. Is buchu really worth its listing? Its old friend scoparium is gone. And does the damning statement that "Cubeb has been given by mouth as a urinary antiseptic" justify its retention? But perhaps we had better be careful; some old drugs are showing signs of renascence; witness the recent studies of the oxytocic action of infusion of raspberry, and the triumph of rauwolfia. Maybe the Revision Committee and their many subcommittees know best; the list of distinguished names makes it difficult to say who would know better.

1. *British Pharmaceutical Codex 1954*. 1340 pp. 63 shillings. Published by direction of the Council of the Pharmaceutical Society of Great Britain. The Pharmaceutical Press, London, W.C. 1, 1954.

OF GEESE AND MEN

There might not seem at first sight to be much connection between the life of the greylag goose and human psychology. There might seem little excuse for mentioning a lecture on geese in a medical journal, but there is a connection nevertheless. On November 29, we had the privilege of hearing a lecture by a distinguished medical truant, Professor Konrad Lorenz, who started by taking an M.D. at the University of Vienna in 1928, then worked for a Ph.D., became a comparative anatomist, a psychologist, and finally an authority on animal behaviour. Professor Lorenz's work reached a very wide public when his first book "King Solomon's Ring" was translated into English and became a Book Society Non-Fiction choice.* The relationship of his work to medicine was recognized by the World Health Organization in 1953 when he was asked to participate in a study group in Geneva on the psychological development of the child, and proved a star attraction.

The good offices of the Royal Canadian Institute were responsible for his appearance at a public gathering in Toronto during his first tour of this continent for many years. Genial, charming and dynamic, the bearded biologist who has learned to talk to animals held a large audience entranced for an hour while he expounded the behaviour of the greylag goose, illustrating his lecture with films and pantomime.

He began by saying that the behaviour of animals is understandable only if their normal behaviour can be observed in a natural habitat. The alternative—laboratory study—is of little value. Fortunately, it is easy to keep some animals in full freedom and yet in close relationship to human observers.

The greylag goose can be made tame by a process known as "imprinting." It has been found that if a human being is the first object seen by the newly-hatched gosling, it will accept this person as a mother object. A few minutes of handling and talking suffice to enrol the observer as an honorary goose, and from then on the gosling will behave towards that person as if he were a parent, at least until full development is reached in two years. The observer therefore has a unique opportunity of observing such things as the unlearned responses to warning calls. An interesting fact elicited was that the angle subtended at the gosling by the "parent" determined the distance at which the bird followed. When the "parent" was upright, the gosling remained some feet behind; when he got into water and swam, the gosling closed up the gap. When the "parent" rode a bicycle, the gosling took to the air; when he lay flat, it landed.

Dr. Lorenz also showed features of reproductive and aggressive behaviour, to illustrate the complexity of social activities in geese.

It is very interesting to speculate on the implications of such studies for human behaviour. For instance, can imprinting occur in babies? Ought the mother to be the first person the baby sees? And is this an additional argument for rooming-in? Here is a nice field of study for the child psychologist.

*His second book, *Man Meets Dog*, has recently been published. In it, he develops his ideas on dog behaviour.

STATISTICAL STUDIES OF MENTAL ILLNESS

Extensive statistical and genetic studies of mental and emotional illness have not been frequently published in the last quarter century. This fact is apparently the sad result of the *overselling* of environmental, interpersonal and "emotional" stresses as the root of all ills. This unhappy tendency has shown evidence of coming to an end in recent years. The pendulum would appear to be swinging back to a more reasonable position, in which no stress of importance as a component of causation is excluded because of adherence to a purely "psychogenic" or "psychodynamic" frame of reference.

One stress which is *always* present is the constitutional and genetic predisposition. This can be statistically determined in many psychiatric illnesses, and may even be the major component in etiology. A number of psychiatrists today are somewhat reticent to express much opinion about this particular aspect of causation, because they are loath to be accused of superficiality, of ignorance of "psychodynamics," and in the long run they are afraid of "losing face" by the censure of their "more informed and initiated" colleagues. Psychodynamic theory has an "answer" for all causes and motives in normal or abnormal thinking, feeling, and behaviour. In actual fact, most of the psychodynamic "causes" in mental and emotional illnesses are not causes at all, but *results* – mechanisms that play a part in the genesis of psychiatric illness, but are not the basic etiological factors. Because of impaired biological function on the basis of constitutional-genetic and/or physiological disorder within the particular patient concerned, the individual is incapable of surmounting the environmental and interpersonal obstacles in his path, whether these obstacles be called stresses, conflicts, or whatever you will. This "incapability" is composed of motives or dynamics.

It is stimulating indeed to see some really solid non-verbal research work going on in psychiatry today. Many advances are being made in the fields of somatic therapy and physiology, which will lead in time to the solution of some of the thorny problems of causation in psychiatry.

In recent years, several excellent publications in English have been produced which deal with the role of genetics in psychiatric illness. The most notable of these in book form are by Kallmann[1] in the United States, and Slater[4] in England, who both used the twin study method. Studies in European languages have been more plentiful.

Sweden offers a favourable research area for population and family investigations in the field of psychiatry. A survey of methods used in Sweden has been published by E. Strömgren.[5] For over 200 years, carefully compiled statistical data of mental illness have, by law, been recorded in the parish registers. The population is relatively homogeneous, and social-economic class differences are comparatively small. Professor T. Sjögren and his colleagues at the Karolinska Institute and the University of Stockholm have previously published studies on the statistical and genetic aspects of psychiatric illness in Sweden.[3] The most recent one, from the Karolinska Institute, will now be briefly discussed.[2] The entire investigation will be published in two parts, this being the first, which is complete in itself.

The material examined covers 45 years of registration for a rural Swedish area with about 25,000 inhabitants, and includes 1,312 registered cases of psychosis, severe psychopathy, low-grade oligophrenia (idiots and imbeciles), and suicide. The limits of these diagnostic terms are defined in the text. A summary of some of the statistics presented by these authors will be of interest.

For 34.2% of the psychotic probands and secondary cases, the diagnosis was schizophrenia, for 18.1% it was manic-depressive psychosis, for 14.9% senile or presenile psychosis, for 18.1% some other specified diagnosis and for 14.7% "undiagnosed psychosis"; 54.7% of the psychotics were women, and 62.2% of the oligophrenics were men.

A diagnosis of low-grade oligophrenia was added to that of schizophrenia in 10% of cases, leading the authors to assume a definite coincidence between the two conditions. Epilepsy as a complication of oligophrenia was found in only 4%. This low figure is contrary to the usual statement that epilepsy is a common complication of oligophrenia.

The total morbidity-risk for schizophrenia was 1.6% for both men and women; for manic-depressive psychosis 0.9% for men and 1.2% for women; for presenile psychosis 0.7% for men and 1.0% for women; for senile psychosis up to 80 years, about 0.6% for men and 0.8% for women; for other psychoses 0.9% for men and 1.1% for women. The aggregate morbidity-risk for all forms of psychoses was thus about 4.7% for men, and 5.7% for women.

The morbidity-risk for low-grade oligophrenia (idiocy and imbecility, upper limit I.Q. of about 55) was 1.0% for men and 0.75% for women. Only very severe, hospitalized psychopaths were included in the study, and the figures were therefore a poor index of frequency—the morbidity risks being very low, 0.35% for men and 0.2% for women. The suicide morbidity risk for the *whole kingdom* calculated for the "normal" years 1921-1930, was 2.67% for men and 0.57% for women. The suicide morbidity risk in the *rural* area studied was lower, 1.75% and 0.23%. Hanging was the most popular method.

This study by Larsson and Sjögren is to be highly recommended for those physicians and sociologists interested in the genetics of mental illness. It is a fine example of careful, accurate medical reporting.

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2. LARSSON, T. AND SJÖGREN, T.: A methodological, psychiatric and statistical study of a large Swedish rural population. Translated by Donald Burton. Acta Psychiatrica et Neurologica Scandinavica. Supplementum 89. Ejnar Munksgaard, Copenhagen, 1954.

3. SJÖGREN, T.: Gentic-statistical and psychiatric investigations of a West Swedish population. Acta Psychiatrica et Neurologica Scandinavica. Supplementum 52. Ejnar Munksgaard, Copenhagen, 1948.

4. SLATER, E.: With the assistance of Shields, J. Psychotic and neurotic illnesses in twins. Med. Res. Council Special Report Series No. 278. Her Majesty's Stationery Office, London, 1953.

5. STRÖMGREN, E.: Statistical and genetical population studies within psychiatry. Methods and principal results. Congrès International de Psychiatrie, Paris, 1950. VI. Psychiatrie Sociale Génétique et Eugénique. No. 1101. Hermann, Paris, pp. 155-188.

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Men and Books

ACROMEGALY AND DR. MARK

S. S. B. GILDER, M.B., *Toronto*

ON FEBRUARY 4, 1855, an individual was born whose chief claim to fame is that he later developed acromegaly and left us a detailed account of his sufferings. Dr. Leonard Portal Mark was the son of the British Consul at Marseilles and was educated in France and at St. Bartholomew's Hospital, London, which he later served as Draughtsman of Pathology—a forerunner of our present race of medical illustrators.

Dr. Mark, who in spite of his acromegaly lived to the age of 75, appears to have been a charming Victorian gentleman, bilingual in French and English, cultured, of considerable artistic talent, and with a good athletic background in his youth. After qualification and the completion of his intern appointments Dr. Mark seemed destined to become a fashionable London practitioner. In his book, "Acromegaly. A Personal Experience," he shows how this pleasant outlook was marred by the insidious onset of acromegaly, which gradually took from him much of the enjoyment of life. He begins his book by saying: "When Fate, shaping my 'ends,' decreed that I was to suffer from the malady Acromegaly (*akra* = ends, *mega* = big), she perhaps gave me the greatest compensation possible by causing me to enter the medical profession. After the distress caused by the one and the enjoyment due to the other—both extending over more than a quarter of a century—I find myself in the unique position of being able to relate a personal experience of this rare complaint as it affected one with some medical knowledge."

There are several interesting features of this book. In the first place, it did not appear until 1912, when Dr. Mark had had the disease for some 30 years, because for a very long time the sufferer failed completely to diagnose his own case. Fortunately, he had, as a good Victorian, kept a diary from the age of 14 and was able in retrospect to place the date of commencement as 1879 when he was a man of 24. It must be remembered, of course, that the condition was described by Pierre Marie of Paris only seven years later, in 1886, but the striking appearance of acromegalics ensured a rapid diffusion of knowledge of Marie's contribution.

Although Dr. Mark took about 25 years to diagnose his own condition, others had been aware of it for some years. It was probably first discovered by a friend, Dr. Lloyd, who had to give Mark gas for a dental extraction and called the attention of the dentist to the typically acromegalic lower jaw. A little later, Dr. Archibald Garrod, the Barts' physician, made the diagnosis in a teashop. Most dramatic of all, Pierre Marie himself picked Mark out of a crowd at an Anglo-French Medical Congress in London as a typical acromegalic. Yet nobody thought of telling poor Mark what was the matter with him though he had an impressive list of symptoms for which he consulted medical colleagues fairly frequently. Some, of course, assumed that the diagnosis was so obvious that Mark must be aware of it. For example, his brother-in-law, who had been let into the secret, called on him one day and discovered a reprint of an article on acromegaly lying on Mark's table; he drew the natural conclusion that Mark had been studying his own case.

The most astonishing feature of the situation is Dr. Mark's own diagnostic blindness, in spite of a very human preoccupation with his many disabling symptoms. He says, "For some 15 or 20 years, each day when I looked into the glass to brush my hair or to shave, there was a typical acromegalic literally staring me in the face. Yet I never recognized the fact." He had noticed for years that his hands were getting bigger, yet he never guessed the reason. When he got out his last winter's gloves, and was unable to get them on, he assumed that they had shrunk in the interval. He had arguments with his bootmaker because his boots appeared to shrink, and this malady unaccountably afflicted his hats as well. The progressive protrusion of the lower jaw made it impossible to chew anything, and his dentist had to fit a denture over the upper teeth to establish contact with the lowers. He remarks that he lost his ability to whistle, and also that his enlarged tongue interfered with his breathing at night (indeed, it almost led to his death under general anæsthesia). And still the diagnosis eluded him.

At last, one day when he was already 50, the diagnosis came to him while he was walking in the street. He at once discovered that his secret was a *secret de polichinelle*, and was at first somewhat annoyed at the attitude of his friends. He says, "I felt somehow that I had been duped, that things which I ought to have known, and which by right were mine, had been kept from me. I am glad to say that this feeling passed away in a few days, and I realized that my friends acted for the best." "Every day since then I . . . . have been more and more convinced that I got my knowledge quite soon enough."

There are some interesting points of ethics arising from this story. Resisting the temptation to reopen the question of the patient's right to know the truth, we may however note the relation of this case history (which, by the way, includes such classical symptoms as headache, visual disturbances, increasing weakness, and disturbance of sleep rhythm) to the common insistence on early diagnosis. Here is the extraordinary spectacle of an intelligent and well-read clinician failing to make a diagnosis which a final-year student should be able to make at a glance. Dr. Mark sums up the situation with one of his

characteristic touches of humour. "We often pray for 'the gift to see ourselves as others see us.' A vain prayer, methinks, when we realize how blind we would still be if it were granted."

To close the story, it should be recorded that from the time when Dr. Mark made the diagnosis to the end of his life at the age of 75 he devoted much of his time to attempts to further the knowledge of acromegaly. His name should be added to the roll of those who out of affliction have drawn profit for their fellow-men.

GENERAL PRACTICE

THE G.P. AND THE MEDICAL SCHOOL

IN A RECENT ISSUE of the *Journal of the American Medical Association* (156: 95, 1954), Dr. Dimond of Kansas City gives a stimulating account of the way in which the University of Kansas Medical School is trying to accomplish the invaluable work of bringing the general practitioner and the undergraduate together.

This is done by means of extramural and intramural preceptorships. In order to give the student of medicine first-hand experience of family practice, every senior student is required to spend five or six weeks under the instructions of a general practitioner practising alone in a town of 2,500 population or less. The student receives room and board, preferably in the physician's home, but no salary. The preceptor must take the student everywhere with him, but is not allowed to send him out alone on calls.

In order to give city G.P.'s a share in the teaching, a panel of intramural preceptors has been set up; these men staff outpatient medical clinics to which students are assigned. Apparently, in spite of the extra trouble involved for extramural and intramural preceptors, there is no difficulty in finding sufficient practitioners to take on the good work. Figures quoted for new entries to general practice in Kansas suggest that this integration of medical school and family doctor has benefited the whole area as regards availability of medical care.

Concurrently with this programme, there has been an increased desire on the part of general practitioners for postgraduate education. Last year, no less than 49 of the 62 preceptors took a postgraduate course at the University of Kansas Medical Center; in addition, 489 practitioners enrolled in circuit courses conducted by university staff throughout the State.

Lastly, the University of Kansas has wisely put a general practitioner on the full-time staff to co-ordinate these activities.

Programmes such as the Kansas one should be studied by medical educators everywhere, so that a satisfactory pattern of integration of the family physician into undergraduate education, from which he has been unfortunately excluded since the days of medical apprenticeship, may be evolved and generally accepted.

MEDICO-LEGAL

WHO DEFENDS THE DOCTOR'S ESTATE?

T. L. FISHER, M.D.,* *Ottawa*

ON MAY 8, 1953, an anæsthetist was called upon to anæsthetize a 31-year-old male patient. He decided to use an intratracheal tube, not one with a collar which could be inflated but an ordinary straight one around which he packed vaseline gauze. The anæsthetic and operation were uneventful, the intratracheal tube was removed and the patient sent back to the ward where, very shortly after, he died. During the night the anæsthetist was killed in a motor accident. Whether or not he knew that his patient had died, he could not have known that the autopsy showed death to have been due to asphyxia from the vaseline gauze, which had not been removed at the end of the anæsthesia.

The patient had been married and supporting a wife and a child one and a half years old. His average income had been about $2,500 a year and shortly he was to have been promoted to a position with a salary of about $3,000 a year. The anæsthetist had been a full-time employee of a group of anæsthetists and had been working with the group since August 1952. At first it seemed that the widow's claim might be made only against the estate of the deceased anæsthetist but later both the estate and the employer, the anæsthetists' group, were included. It looked at first as though the claim might be about $12,000 but soon this was raised to $25,000. The nature of the accident made a successful defence doubtful, and owing to the death of the anæsthetist it was almost certain that any defence would be unsuccessful.

After some negotiations the widow made a firm offer of settlement for $20,000 plus $3,000 legal fees. There was little doubt that a court award would have been at least as great. In the same province a case involving the death of a wage-earner had been defended unsuccessfully a short time before, damages twice as high being awarded. Having in mind the differences

*Secretary-Treasurer, Canadian Medical Protective Association.

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between the two cases, the widow's offer seemed as good as could be expected from a court award and it was accepted. Legal expenses were not quite so high as had been anticipated, amounting to $2,536.50 instead of $3,000. Thus the total cost of the case was $22,536.50.

Over the years the Canadian Medical Protective Association has adopted as a principle of action that all cases which can be defended should be defended. Every settlement increases the risk of demands on other doctors in the same district, and unnecessary settlements are potentially more harmful. Yet there are some cases, of which this is an example, in which no adequate defence is possible. Provided the demands of the plaintiff are not unreasonable, the more promptly the settlement is reached the better.

A few years ago the Canadian Medical Protective Association thought that the estate of one of its deceased members was going to be sued. At that time there was no provision in the by-laws of the Association whereby it could assist. Such provision was made. In the three years since, two estates, the one involved in the case reported above and another, have been given help. In the second case action had been begun against a member just before his death, the case went to court and damages of $3,000 were awarded the plaintiff. This case is being appealed.

The knowledge that liability for the results of malpractice or negligence extends to the estate of a deceased doctor suggests the need for taking advantage of the retirement fee whereby the Canadian Medical Protective Association provides membership for retired doctors or for their estates after their death.

MISCELLANY

BLOOD FRACTIONATION BUILDING, TORONTO

Since April 1953 the fractionation of blood has been conducted at Connaught Medical Research Laboratories, University of Toronto, to yield gamma globulin which has been used to minimize the paralytic effects of poliomyelitis. Limitations of equipment and space precluded the possibility of doing more than preparing gamma globulin and holding the other fractions of blood in refrigerated storage for future use. However, on October 9 the Honourable Paul Martin, Minister of National Health and Welfare, opened at the Dufferin Division of Connaught Medical Research Laboratories a building equipped to provide adequate facilities for the fractionation of human blood into a number of clinically useful components.

The Blood Fractionation Building is a single-storey, red brick structure with silvery-grey limestone trim. It has a floor area of approximately 12,000 square feet. The main processing equipment is located in two refrigerated laboratories having a total area of approximately 2,000 square feet. Four high-speed refrigerated centrifuges for the separation of various fractions of plasma are located in the −5° C. laboratory. The use of standard partitions and other features in the planning have made it possible to provide additional facilities for increased production in the event of a national need.

The raw material for the fractionation process consists of human blood, human plasma or human serum provided by voluntary donors through the facilities of the Canadian Red Cross Society. Monthly deliveries from the Society amount to about 12,000 donations but at times approach 15,000 donations. The opening of this building, and the opportunity which is presented thereby, are a challenge to Canadians to support the Society's blood donor programme.

The process used for the separation of human blood into its various components is based upon the excellent work in the field of physical chemistry by the late Professor Cohn and his associates at Harvard Medical School. It depends upon the solubility of fractions of blood in various concentrations of alcohol and at various ionic strengths and acidities at a temperature of −5° C.

The product at present being produced is gamma globulin (immune serum globulin) which has uses in the fields of poliomyelitis, measles, mumps, infectious hepatitis, hypogammaglobulinæmia and German measles. At present, distribution of the finished product is confined to the first of these fields. Serum albumin for use in treatment of shock and burns is also being produced and distributed through the Canadian Red Cross Society. Fibrinogen will be available within a few weeks. The building will be operated under the general direction of Mr. M. D. Orr, Assistant Director of the Laboratories. Dr. Arthur F. Charles will give immediate direction to the fractionation procedures and Dr. A. M. Fisher will continue his close association with the blood programme. A staff of about fifteen persons will be employed.

The opening of the Blood Fractionation Building marks another step in providing in Canada adequate facilities to make full use of developments in the field of medical research, to make the products of research in blood fractionation available for the health and welfare of Canadians in peace and war, and to provide opportunities for extension of research in this field.

The programme has been truly national through the application of funds provided by the Department of National Health and Welfare, Ottawa, for the National Health Grants and the co-operation of the Governments of each of the Provinces in the expenditure of those grants. Eight of those Provinces were represented at the opening ceremonies by their Deputy Minister of Health.

The building site, auxiliary services, and administrative direction have been made available by Connaught Medical Research Laboratories, University of Toronto.

Thus the Canadian blood fractionation programme is a result of co-operation between the Department of National Health and Welfare, the various provincial departments of health, the Canadian Red Cross Society, and the Connaught Medical Research Laboratories.

THE HANDICAPPED CHILD

Dr. Karl König, who is an exponent of the Rudolf Steiner system, has produced the first of a series of booklets in the form of letters to parents of handicapped children. His first booklet (*The Handicapped Child*, I) consists of three letters from a therapist to the relatives of a mongol, a spastic child and an autistic child, giving general advice and explanation of the situation. The booklet is obtainable, price one shilling and sixpence, from New Knowledge Books, 28 Dean Rd., London, N.W.2, England.

Association Notes

South on University Avenue from portico of Parliament Buildings.

CONJOINT B.M.A.-C.M.A.-O.M.A. MEETING, TORONTO

THE PREPARATION of the scientific programme for the Conjoint Annual Meeting of the B.M.A., C.M.A. and O.M.A. in Toronto, for the week beginning June 20, is well advanced. The need for arranging a programme by postal consultation across the Atlantic naturally delays matters, though we are happy to say that the edges are being rounded off nicely in most of the 16 Sections, and we hope to print a complete programme next month.

It is 25 years since we last had the pleasure of entertaining members of the British Medical Association at an Annual Meeting. On that occasion, in late August 1930, in Winnipeg, the Canadian Medical Association had been affiliated to the British body for only six years, and the relationship, as expressed by the then President, Dr. W. Harvey of Winnipeg, was still looked on as that of mother and daughter (with the Canadian daughter a married woman and therefore head of her own house.) Perhaps it is not uncomplimentary to suggest that the mother has undergone some rejuvenation—as is the fashion of modern mothers—while the daughter has matured, so that now to the casual observer they appear more like sisters—again quite a modern phenomenon.

We wonder whether the 1930 figure for attending British physicians will be exceeded in 1955. At the Winnipeg meeting, out of a total physician registration of 1,602 there were 303 physicians from the British Isles and 214 from the United States. But that was in an age of open frontiers and British prosperity.

And what were Canadians discussing in 1930? Why, the St. Lawrence Seaway. In an article to

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the *British Medical Journal*, Dr. D. A. Stewart wrote that "the building of large canals to bring ocean vessels to Lake Superior and the very heart of the continent is Canada's next big job." We will be able to tell our guests this summer that the job is at last in hand, and it is understood that it may be possible to present them with a handsome brochure illustrating this great project.

In Britain and in Canada, they were already discussing a subject still topical—the question of national health insurance. This journal commented in August 1930 on a report which had just been published by the British Medical Association on national health insurance. As the Canadian Medical Association has done since, the B.M.A. affirmed its acceptance of the principle of prepaid medical care, and gave its views on insurance practice.

The turn of events in Great Britain has produced a very different type of health insurance from that envisaged by the doctors in 1930. We shall have the details of this National Health Service explained to us by qualified spokesmen at the Toronto meeting in June. It is certain that their expositions will not lack for hearers. Will you be there? We hope so.

SCIENTIFIC EXHIBIT

Scientific and research groups are reminded that arrangements are well in hand for the usual scientific exhibition, but that there is still room for additional exhibits. The presence of our visitors from the United Kingdom should be an added incentive to Canadian scientists to display their work.

HOUSING APPLICATION FORM

CONJOINT MEETING — B.M.A - C.M.A - O.M.A.

Toronto, June 17 - 24, 1955

(Scientific Sessions, June 20 - 24)

Reservations now being accepted

MAIL THIS APPLICATION

To:
GLENN SAWYER, M.D.,
CHAIRMAN, COMMITTEE ON HOUSING,
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Date of arrival ..... A.M. / P.M. Departure .....

Room will be occupied by:—

Name — Street Address — City — Province

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Send confirmation to: .....
(Please print)

Street .....

City .....

Province .....

MEDICAL SOCIETIES

THE FEDERATION OF MEDICAL WOMEN OF CANADA

The following events are being arranged in connection with the conjoint Annual Meeting of the Canadian Medical Association and British Medical Association in June next:

1. Tea at the home of Dr. Marion Hilliard, Sylvan Avenue, Scarborough, at 5.00 p.m., June 19, following the church service.
2. Annual meeting of the Executive at the Royal York Hotel at 9.00 a.m., June 21.
3. Reception for the British women delegates at the home of Dr. Lillian Lome, 21 Woodland Heights, at 5.30 p.m., June 21, followed by
4. Annual dinner at the Old Mill, 21 Old Mill Road, at 7.30 p.m., June 21.

MEETING OF QUEBEC ASSOCIATION OF RADIOLOGISTS

At a meeting held on November 6 at the Queen Elizabeth Hospital, the Association of Radiologists of the Province of Quebec elected its executive committee for 1954-1955. *President*—Dr. Donald McRae (Montreal Neurological Institute). *Vice-president*—Dr. Henri Lapointe (St. Enfant Jésus Hospital, Quebec). *Secretary*—Dr. Jean-Louis Léger, (Notre-Dame Hospital, Montreal). *Treasurer*—Dr. Ivan Vallée (St. Luke Hospital, Montreal). *Secretary of the Meetings*—Dr. Odilon Raymond (St. Luke Hospital, Montreal). *Directors*—Dr. Jules Gosselin (St. Sacrement Hospital, Quebec); Dr. Jean-Pierre Jean (Herbert Reddy Memorial); Dr. Albert Jutras (Hôtel Dieu, Montreal); Dr. E. M. Crawford (Queen Elizabeth Hospital, Montreal); Dr. I. Sedlezky (Jewish General Hospital, Montreal).

CANADIAN COMMISSION ON HOSPITAL ACCREDITATION

The Canadian Commission on Hospital Accreditation held a meeting at 244 St. George Street, Toronto, on December 9, at which their operations during the nine-month working period in 1954 were reviewed. This meeting was of special significance because it marked the close of the first full year of operation, during which 155 Canadian hospitals were visited, as against 90 in 1953.

At the meeting, Dr. E. Kirk Lyon of Leamington, Ont., was elected chairman and Dr. Owen C. Trainor of Winnipeg vice-chairman. Dr. Karl Hollis, who with Dr. J. J. Laurier is acting as surveyor of hospitals, was elected secretary. Rev. Father Hector Bertrand of Montreal is to be treasurer.

The finances of the Commission, which depends for support on the Canadian Hospital Association, Canadian Medical Association, Royal College of Physicians and Surgeons, and l'Association des Médecins de Langue Française, are in good shape, and it will be possible to operate on a twelve-month basis during 1955. It should be emphasized that hospitals are visited without charge by the Commission's surveyors, although the cost of each visit to the Commission is approximately $140. Such visits are not made unless requested by the hospital. It is the sincere hope of the Commission that more and more Canadian hospitals will ask for visits.

Hospitals desiring a visit for the purpose of inspection and possible accreditation should not communicate with the Commission directly, but should apply to the associated body, the Joint Commission on Accreditation of Hospitals, 660 North Rush Street, Chicago, Ill.

CORRESPONDENCE

LEGALIZED EUTHANASIA

To the Editor:

I carefully read three, four and five times the article written by Professor Rowan in the November edition of your journal before realizing the true and full sense of the words used in it. No doubt: A Canadian, a professor in a Canadian university, is deploring the fact that the medical profession, as a whole, has not the right to practise euthanasia. According to Professor Rowan, a great many doctors have an identical viewpoint, but "are individually impotent to do the rational and humane thing because their hands are tied by law." "Who makes these laws"? asks Professor Rowan; and he answers: "politicians."

Poor answer, Professor Rowan. Above the politicians, even above the churches, there is a natural law, the author of which is God. If you do not believe in the existence of God, do not go further, it is useless.

But, I suppose you are intelligent, Professor Rowan, and you believe in a Supreme Being who created the universe. I do not have to prove here the existence of God, but you must admit that each individual in the world, people, animal or thing, has to obey intimate or natural laws before obeying laws made by men. One of those natural laws is the one that forbids the deliberate killing of an innocent human being; that law was reinforced by the Divine commandment: Thou shalt not kill.

The allied populations were horrified when it was heard from Germany that Hitler and his instruments were establishing in their country a kind of euthanasia: sterilization of the tainted, and simple murder of the unemployable and of the unfit. How was that possible? Each time one forgets that a human being has not only a body but also an immortal soul, this terrible thing happens; the people are equated with animals and treated like them and even worse.

You probably found awful the hitlerian methods, and now, Professor Rowan, you ask the medical profession to use the same barbarian way? It is hardly credible. If the principles set forth by Hitler were bad and false, they are also bad and false when they are put forward by you or others; to kill the unfit at forty years of age or at two hours of age is the same thing. From early days until now, the duty of medical men has been to cure the ill, to relieve the suffering and to preserve life by all means; that duty was never to kill, even "for pity's sake." It is the reason why people can have confidence in physicians and put in their hands the most precious thing of all, their life. Otherwise, nobody would go to a doctor for treatment.

About the cases you refer to, many comments could be made. In case A, if, as you say, it was the personal desire and final wish of the woman to have a *coup de grâce*, why ask a doctor to do it? Was she not able to kill herself? If she was not able, she did not have a real desire to die, and in that she was obeying the natural law of conservation. As regards case B, I regret to tell you that it is impossible to say at the time of birth whether a child will be of normal intelligence or

not, even in the presence of the worst deformity; you must have seen some persons with a scarcely human face and yet with normal intelligence. Case C is no better. The imperfect child has the same birthright as his brother and sisters; if his parents were completely innocent, do you think he was less innocent than they of this state of things?

Finally you say, Professor Rowan, that human biology irrevocably controls our ultimate destiny. If you mean our ultimate destiny on earth, that is true. But if you mean that death signifies the very end of everything for human beings, I do not agree, because I still believe the human soul to be immortal.

I have every hope, Professor Rowan, that the men of my profession will ignore your proposal and continue to give the best of their own life to preserve the life of others.

JULES LAVOIE, M.D., F.I.C.S.

St. Georges de Beauce, P.Q.
December 11, 1954.

SPECIAL CORRESPONDENCE

The London Letter

(From our own correspondent)

THE USE OF TRILENE BY MIDWIVES

In March 1949, the Medical Research Council appointed a committee "to advise and assist in promoting research on the possibility of devising improved or new methods of producing analgesia, suitable for use by midwives." The committee, which restricted its investigations to the use of Trilene (trichlorethylene B.P.), has now issued a report in which it "recommends that midwives, acting on their own responsibility, after adequate instruction, be permitted to administer Trilene with inhalers conforming" to a specification laid down in the report.

The evidence upon which this recommendation is based, and which is fully laid out in the report, consists of observations made on 772 domiciliary and 1,328 hospital confinements. A careful perusal of the report suggests that the committee is not particularly enthusiastic in its recommendations, and stringent conditions are laid down for the use of this controversial anæsthetic. One is that "the maximum concentration of Trilene vapour delivered should be 0.5% by volume with a permissible variation of ± 20% of this concentration. The inhalers should be capable of providing as an alternative a weaker concentration of 0.35% by volume, which is adequate for long periods in many cases."

According to the report, the available evidence "seems to show" that these two concentrations are "reasonably safe and effective, but it gives no justification for regarding any higher concentration as safe." Further, "to ensure that inhalers conform to the recommended specification, every inhaler should be tested in the laboratory before being put into service. Periodic checking will also be necessary. Tests should be carried out in an independent laboratory officially approved for the purpose."

THE HEALTH OF THE SCHOOL CHILD

In his report for 1952 and 1953, the Chief Medical Officer of the Ministry of Education reports that in 1953, only 2.2% of the 6,205,988 school children in the country were considered by school doctors to be of poor general condition. Diphtheria is now an uncommon disease: there were only 117 cases in the age group 5-14 in 1953, with seven deaths, and deaths from tuberculosis in this age group have fallen from 973 in 1938 to 107. It is the minor health hazards that give rise to concern. Thus, a survey of 30,000 children showed a substantial increase in dental caries, compared with 1948; for instance, only 12% of the 12-year-old children examined had no decayed, missing or filled teeth. Attention is drawn to the fact that the consumption of sugar per head in this country rose in 1946, and it is suggested that a campaign against the unrestricted consumption of confectionery might lead to a considerable reduction in the incidence of caries.

The number of verminous children is the smallest in the history of the Service—316,854, but, to quote the masterly understatement of the report, "it is disappointing that there are still well over a quarter of a million children with nits or lice." An interesting feature of the report is the "strong plea" that is made for the retention of handicapped children in ordinary schools whenever possible. "The majority of these children," it is pointed out, "will have to enter unsheltered industry on leaving school, and the more accustomed they are to living in a normal environment the more likely they are to become self-reliant men and women."

RESEARCH ON TOXÆMIA OF PREGNANCY

A promising approach to the perennial problem of toxæmia of pregnancy is opened up by the announcement that the Nuffield Foundation has made a grant of £24,500 to Oxford University for research on toxæmia of pregnancy in sheep. Veterinary investigations have shown that toxæmia symptoms, indistinguishable from those of toxæmia of pregnancy, can be induced in pregnant ewes by over-feeding them so that they make large gains in weight, and then suddenly and severely restricting their diet. Preliminary field trials have shown that by limiting weight gain during early pregnancy the ewe mortality can be reduced from 15-20% to less than 1%. The similarity between toxæmia of pregnancy as seen in women and ewes is so marked that it is obvious that this approach in the veterinary field should be adequately followed up, and it is for this reason that the Nuffield Foundation has made this generous grant.

ANONYMITY IN BROADCASTING

The advent of television has added yet another hazard to those responsible for preparing professional ethical codes. Apparently, the British Medical Association has received several complaints recently of medical practitioners allowing their names to appear in published radio programmes or to be announced on the air.

The attention of members of the Association has therefore been drawn to the officially approved "Report of Council on Indirect Methods of Advertising," of which the following are the important sections. Anonymity in broadcasting is defined as "withholding the publication or announcement of the practitioner's name, or any information, such as particulars of the appointments he holds, which might enable the public to identify him. Identification cannot be completely excluded, but it is incumbent upon medical practitioners who take part in sound or television programmes to ensure that the possibility of identification and publicity is reduced to a minimum. . . . Unless a practitioner insists on anonymity he is not only offending against the ethical principles of the profession but is placing himself in danger of being accused of violating the 'Warning Notice' of the General Medical Council. Should a practitioner, while carefully observing these precautions, be recognized by a section of the public, that fact should not of itself be regarded as evidence of an infringement of the rule of anonymity."

The position with regard to commercial radio is that "it is unethical for a practitioner to participate in sound or television programmes which are being presented for, or on behalf of, firms using sponsored radio as a means of advertising."

WILLIAM A. R. THOMSON

London, January 1955.

OBITUARIES

DR. H. HAYS BULLARD, for nine years professor of pathology and bacteriology in the medical school of the University of Western Ontario, London, and chief pathologist at Victoria Hospital, died on December 12 in Wilmington, Delaware. He was 71. Dr. Bullard, who was born in St. Louis County, Missouri, obtained the Ph.D. degree from Tulane University in 1912 and four years later graduated in medicine from Johns Hopkins University. He was resident pathologist at Johns Hopkins Hospital from 1918 to 1920, when he came to Canada to join the staff at the University of Western Ontario. Since his return to the United States in 1929 he had held a number of hospital appointments. He is survived by a son and a daughter.

DR. WILLIAM WILSON CAMPBELL, 29-year-old graduate of the first medical class at the University of British Columbia, died on November 26 while serving his internship at the Vancouver General Hospital. Dr. Campbell, who was born at Ladysmith, B.C., was a veteran of World War II, having served both with the R.C.A.F. and the Canadian Army. He is survived by his widow, his parents, and a sister.

DR. RICHARD COLLIER COATSWORTH, 66, died on December 25 at Sunnybrook Military Hospital, Toronto. Dr. Coatsworth, a grandson of Toronto's first city commissioner, obtained the degree of Bachelor of Medicine from the University of Toronto before going overseas with the R.A.M.C. as captain. In 1918 he was awarded the Military Cross for courage under fire. After the war he did postgraduate work in hospitals in London and Dublin and then became senior intern at a hospital in Canterbury. On his return to Canada in 1920, he interned for a year at the Toronto General Hospital and then took over his father's practice. At that time Dr. Coatsworth began a long association with the Toronto transportation systems, as medical adviser first to the Toronto Street Railway and, later, to its successor, the Toronto Transportation Commission. He is survived by his widow and one son.

DR. JOSEPH E. A. CLOUTIER, of Cap St. Ignace, Que., died suddenly on November 14 at the age of 76. Dr. Cloutier, a graduate of Laval University, had practised medicine at Cap St. Ignace for 51 years. He is survived by his widow, three daughters, and three sons, one of whom, Dr. Louis Cloutier, is on the staff of Laval University.

DR. MORLEY G. CODY, a specialist in pædiatrics, died suddenly in Calgary on December 23 at the age of 69. Dr. Cody, who was born in Newmarket, Ont., graduated in medicine from the University of Toronto. After four years' practice at Mount Albert, Ont., he spent some time in postgraduate work in Scotland, later taking up the practice of pædiatrics in Calgary in 1927. For many years Dr. Cody was medical superintendent of the Calgary Red Cross Crippled Children's Hospital, a position from which he retired in October 1954. In recognition of his 27 years of voluntary service with the Canadian Red Cross Society, he was awarded honorary membership by the Alberta division of the Society. Dr. Cody was also on the staff of the Calgary General Hospital and the Holy Cross Society. He is survived by his widow and a son, Dr. Alan Cody, who has been associated with his father's practice since 1951.

DR. EDWARD WALLER FLAHIFF, 51, died suddenly on December 5 at Kirkland Lake, Ont., where for the past seven years he had served with the Ontario Workmen's Compensation Board, specializing in the treatment of silicosis in hard-rock miners. Dr. Flahiff was born in Paris, Ont. After graduating in medicine from the University of Toronto, he obtained the Diploma in Public Health in 1929, and from 1930 to 1941 served in Jamaica, B.W.I., under the auspices of the Rockefeller Foundation. From 1941 to 1946 he was with the R.C.A.M.C. in Italy, France and Holland. He is survived by his widow and two daughters.

DR. J. N. FORTIN, of Verdun, Que., died in that city on December 17 at the age of 63. He was a graduate of Laval University, Quebec, and had practised in St. Boniface, Winnipeg, Cochrane, Kenogami, St. Jean d'Iberville, and Verdun. For a number of years he had been medical adviser to the home operated by the Little Sisters of the Poor, in Montreal. He is survived by two sons and two daughters.

DR. H. P. GOUTHRO, 82, died suddenly on December 17 in North Sydney, N.S., where he had been living in retirement. Dr. Gouthro, who was born in North Sydney, graduated in medicine from New York University in 1895. At the outbreak of World War I he went overseas with the R.A.M.C., as captain. After the war he served for a time on the staff of Camp Hill Hospital, Halifax, resigning to become chief medical officer with the immigration department, with headquarters in Halifax. He retained this appointment until his retirement in 1932. Dr. Gouthro is survived by his widow and two daughters.

DR. JOHN KING KELLY, who practised at Almonte, Ont., for half a century, died suddenly at his home on November 30 at the age of 80. Dr. Kelly began his medical career after graduating from McGill University in 1896. For some 35 years he served on the medical advisory board of the Rosamond Memorial Hospital in Almonte and for many terms was chairman of the board. He was medical health officer of Almonte for 20 years. He retired from practice in 1945. Dr. Kelly is survived by his widow, a son, and a daughter.

DR. DALTON M. LIVINGSTONE, 66, who had been in general practice at Dundas, Ont., for the past 38 years, died on December 24. Dr. Livingstone, who was born in Collingwood, Ont., taught school before entering Queen's University, where he graduated in medicine. He started practice in Dundas in 1916.

DR. ROBERT JOHN PERCIVAL McCULLOCH, internationally known ophthalmologist, died on December 26 at his home in Toronto. He was 73. Dr. McCulloch was born at Keene, Ont., and graduated in medicine from the University of Toronto in 1904, as gold medallist. After a few years of general practice in Orillia and Belleville, he decided to specialize in ophthalmology and spent three years in London and Vienna in postgraduate study. On his return to Belleville he established practice as a specialist. At the outbreak of World War I he enlisted with the R.A.M.C. and was posted to a base hospital at Calais; later, he joined the staff of the Central Medical Establishment in London. After the war he set up practice in Toronto and became one of the city's leading eye specialists. He was head of the eye department at the Toronto Western Hospital until his retirement seven years ago. In 1934 he went to China under the auspices of the United Church in Canada in connection with eye work in mission hospitals, and a few years later he visited India for the same purpose. For many years he was chief consultant for the Canadian National Railways. Dr. McCulloch is survived by his widow; two sons, one of whom is Dr. Clement McCulloch of Toronto; two sisters, and a brother, Dr. Ernest McCulloch, Toronto.

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DR. GEORGE W. MacNEIL of Pontypool, Ont., died suddenly on November 23. At 62, he was one of the last country doctors in the Pontypool-Bethany area, near Peterborough, where he had lived since he took over the practice of the late Dr. D. W. Clark in 1923. After graduating from the University of Toronto in 1915, he served for four years as a medical officer in World War I. After World War II he was an associate doctor at the Department of Veterans' Affairs hospital in Peterborough. He is survived by two sisters.

DR. J. A. SEGUIN, head of the anæsthesia department of Verdun General Hospital, died suddenly in Verdun on November 27 at the age of 53. Dr. Seguin was born at St. Clet, Que., the son of Dr. and Mme. Ludger Seguin. After graduating in medicine from the University of Montreal, he began general practice in Verdun. In January 1953 he received the hospital appointment. He is survived by his widow, two sisters, and a brother, Dr. Fernand Seguin, of the Hôtel-Dieu Hospital, Montreal.

DR. JAMES ERNEST SPANKIE, who started his medical practice among the hard-rock miners in British Columbia's early days, died in Vancouver on November 15 at the age of 83. After graduating from Queen's University in 1891, he worked at Banff under Dr. R. G. Brett, who later became Lieutenant-Governor of Alberta. In 1899 Dr. Spankie moved to Greenwood, B.C., to set up practice among the miners of the small town. After ten years in Greenwood he moved to Vancouver, where he continued in practice until his retirement two years ago. In 1950 he was made a life member of the British Columbia College of Physicians and Surgeons. He is survived by his widow and a son.

DR. CHARLES ALGERNON DE VESCI TEMPLE, 84, died at Sunnybrook Hospital, Toronto, on November 22. He was born in Toronto, son of the late Dr. James Temple, and was a graduate in medicine of Trinity College, Toronto, of which he was the oldest surviving graduate. He practised medicine and surgery in Toronto for 40 years. Since his retirement 14 years ago he had lived in Unionville. During World War I he served in France with the 4th Field Ambulance as captain. He is survived by his widow and a daughter.

DR. ALFRED WADE TREFRY, 68, died on November 16 at St. Anne's Military Hospital, Montreal. Dr. Trefry, a native of Yarmouth, N.S., settled in Montreal after serving with the R.A.M.C. during World War I. He was a member of the staff of the Montreal Health Department for 13 years until illness compelled his retirement in 1951. He is survived by his widow and three daughters.

DR. ISABELLA S. WOOD, who practised medicine in Toronto for more than 50 years, died at the Women's College Hospital on November 29 after a short illness. Dr. Wood graduated from Trinity Medical College in 1903 and took postgraduate work in Boston and Saint John. During her practice she had been connected with St. Michael's Hospital, Toronto Western Hospital, and Women's College Hospital, and was widely known for her work among mothers and children. She had been secretary of the Inter-Church Medical Board and a member of the Church Board of Medical Examiners. Dr. Wood was a member of the Canadian Medical Association, the Ontario Medical Association, and the Academy of Medicine, Toronto. She is survived by a brother.

ABSTRACTS *from current literature*

MEDICINE

Sarcoidosis with Involvement of Nervous System.

HOOK, O.: ARCH. NEUROL. PSYCHIAT., 71: 554, 1954.

The author reports on nine cases of sarcoidosis with involvement of the central nervous system; in seven of these cases the neurological symptoms were the presenting ones. A follow-up examination was made, and it was found that all the patients (except one who had died of an intercurrent disease) were alive, the average follow-up period being five years. Five patients exhibited mild or severe mental symptoms; in one patient with progressive symptoms commitment to a mental hospital was necessary, one patient was hallucinated for a few days, and another had progressive mental deterioration which was alleviated by surgical treatment of an obstructing lesion in the temporal lobe. Symptoms resembling those found in cerebral tumours were also found; one patient developed a homonymous hemianopia which was found to be due to involvement of the frontal and temporal regions, one patient developed diabetes insipidus, another had sleep disturbance and two other cases had paræsthesiæ. The author points out that sarcoid lesions have been previously described as occurring in the meninges, but granulomatous masses in the choroid plexus have not been observed previously; involvement of the pituitary gland appears to be especially common. Other authors have described epilepsy, unilateral sensory defects, extrapyramidal syndrome, cerebellar defects and variable disseminated cerebral symptoms.

The facial is the cranial nerve most commonly affected; this occurred in four of his nine cases. The idea of local pressure on the facial nerve by the enlarged parotid gland is an incorrect one, because facial paralysis may occur in the absence of a parotid lesion. He comments on involvement of the eye in this disease, one of his cases having a recurrent papillitis and another an Argyll-Robertson pupil. In the cerebrospinal fluid a marked pleocytosis and elevated protein level were found in only two patients, but in four other patients there was a slight pleocytosis. The author concludes with a discussion on the diagnosis and differential diagnosis of the disease.

W. F. T. TATLOW

The Long-term Prognosis Following Myocardial Infarction and Some Factors Which Affect It.

COLE, D. R., SINGIAN, E. B. AND KATZ, L. N.: CIRCULATION, 9: 321, 1954.

This study was undertaken to establish the long-term prognosis of the initial attack of myocardial infarction. For this purpose, 285 patients who had their initial attack between 1932 and 1942, and who survived the first two months, were followed until their demise or the end of the study (January 1, 1952). Some of the factors which determine long-term survival were analyzed.

It appears that the life expectancy following recovery from the *first* attack of myocardial infarction is better than had previously been reported. In this series, two-thirds of the 285 patients who recovered survived more than 5 years, two-fifths lived over 10 years, and one-tenth lived more than 15 years. The average survival time, including patients who were still alive at the end of the study, was more than 8 years. The immediate mortality during the first two months after the attack was 23%.

The following factors were found to affect the prognosis:

Age. The long-term prognosis was better in younger patients. This was true of females as well as males. *Hypertension* before or during the attack had no effect on the immediate mortality, but its absence definitely increased the long-term survival. *Diabetes mellitus* had no augmenting effect on the immediate mortality, but its presence was a factor against long survival. Female diabetics lived longer after infarction than did male diabetics.

Angina pectoris was present in 60% of the cases prior to the first infarct. In patients who had angina for at least a year before infarction there was a reduced immediate mortality and an increased chance for long survival, as compared with those who had angina for a shorter time. The reason for this is not clear, but is probably associated with the development or non-development of compensatory collateral circulation. *Congestive heart failure* during myocardial infarction definitely augmented the immediate mortality and diminished the chances for long-term survival. *Shock* affected the immediate prognosis of the acute attack in the same way as did congestive failure. However, unlike heart failure, shock had no effect on the long-term survival. *Pulmonary embolism* was an important factor in increasing the immediate mortality, and practically excluded the possibility of prolonged survival. The presence of *gallop rhythm* during the attack indicated a poor prognosis both for immediate and for prolonged survival.

Pericarditis had a negligible effect on immediate and long-term prognosis. Patients who were at rest at the time of onset of a myocardial infarction had a worse prognosis for immediate and for prolonged survival, as compared with those who were exercising or under emotional stress at the time of the attack. Individuals who used tobacco or alcohol prior to the infarction did not have any worse prognosis than abstainers. Body build had no apparent effect on prognosis. Elevation of non-protein nitrogen at the time of infarction can be considered definitely a bad prognostic omen for immediate survival. Both the immediate and the long-term prognosis was better in those who had a low average white blood cell count during the first week following infarction than in those with a high count. Analysis of the electrocardiogram showed that infarcts of the anterior wall had a better immediate prognosis than those of the posterior wall; the long-term prognosis in the two varieties was the same. The presence of ectopic rhythms did not increase the immediate mortality but decreased the possibility of long-term survival.

After careful consideration of all prognostic signs, it is suggested that the best index to prognosis after recovery from a myocardial infarction is the ability of the patient to resume activity. Almost two-thirds of the survivors in this series were able to return to moderate or complete activity after recovery from the first attack of myocardial infarction. The study suggests that the long-term survival time of a recent myocardial infarction is better than that previously estimated, especially for the first episode. S. J. SHANE

Cerebral Metabolic Disturbances in Hypothyroidism.

BROWNING, T. B., ATKINS, R. W. AND WEINER, H.: ARCH. INT. MED., 93: 938, 1954.

The authors have reviewed the literature on the psychoses occurring in hypothyroidism from the original monograph by Sir William Gull to the present day, and continue with their observations on seven psychotic hypothyroid adults with delirium. Whereas in all other forms of delirium the electroencephalogram shows a decrease of frequency and increase in voltage, in hypothyroidism there is both a slowing of frequency and a decrease in amplitude voltage. The authors consider that these electroencephalographic changes are due to an impaired state of cerebral metabolism, evidence of such a state being obtainable from the clinical examination and by the nitrous oxide technique. Thyroid therapy produced both a clearing of the delirious state and an improvement in the electroencephalogram; the authors conclude from this improvement that the thyroid extract reversed the cerebral metabolic defect. It is pointed out that the psychiatric effect of myxœdema on an individual probably depends on individual factors, and the authors believe that the psychosis of myxœdema is fundamentally a delirium and not a specific and separate entity such as the "functional" psychoses. Of some interest is the fact that the delirium may be very mild in hypothyroid patients, and may be the only clinical manifestation of their condition. W. F. T. TATLOW

SURGERY

A Comparison of Intra-arterial and Intravenous Transfusion in Normal Dogs and in Dogs With Experimental Myocardial Infarction.

HAMPSON, L. G., SCOTT, H. J. AND GURD, F. N.: ANN. SURG., 140: 56, 1954.

Dogs surviving for seven weeks after ligation of the descending branch of the left coronary artery were subjected to experimental shock by bleeding from the femoral arteries. Resuscitation by intravenous and intra-arterial transfusion was carried out on each dog. It was concluded that if the rate of transfusion was the same for both transfusion routes, the response was equally good whether it was venous or arterial. Control animals without myocardial infarction responded similarly. Rises in venous pressure were no greater with intravenous than with intra-arterial transfusions given at the same rapid rate. Overtransfusion was foreshadowed by a fall in arterial blood pressure and a simultaneous rise in venous pressure, whatever the route.

In the correction of hæmorrhagic shock, rapid intravenous blood transfusion would appear to be the resuscitative method of choice. BURNS PLEWES

A Study of the Deaths Associated with Anæsthesia and Surgery.

BEECHER, H. K. AND TODD, D. P.: ANN. SURG., 140: 2, 1954.

To find out whether anæsthesia has an unnecessarily high death rate and because knowledge of the dangers is inadequate, a study of 600,000 anæsthesias in ten American university hospitals from 1948 to 1952 was made. All deaths on the surgical services were examined. The study represents an enormous amount of work by many physicians and surgeons.

In these hospitals a fifth of the anæsthetics were given by nurses, but over the five years the proportion decreased by 4%. Only very few anæsthetics were given by the occasional physician. Inhalation anæsthesia was the commonest (about half); intravenous was increasing, and spinal was used in only 9%. The use of ether increased to 62% during the five years and the use of cyclopropane decreased slightly. Spinal anæsthesia was accomplished with Pontocaine in 85%; the use of Nupercaine decreased steadily, and continuous spinal techniques declined. It is noted that endotracheal intubation showed an increasing use of inflatable cuffs; two of the 384 anæsthesia deaths were due to cuffs. Curare (including all muscle relaxants used) was difficult to assess, for data appeared to make its use much more dangerous than was likely; e.g., deaths during induction were 1:2,000 when curare was used and 1:15,500 when not used. The finding of a mortality six times greater when relaxants were used is carefully considered, and it is demonstrated that it is not related to "poor risk" patients, and that physician-anæsthetists have the same mortality rate with curare as do nurses. Evidence is presented that the curare drugs have an inherent toxicity; this toxic

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effect is more evident in men, or women are more tolerant. It is suggested that the present criticism of Pentothal could be more justly applied to curare.

Anæsthesia deaths affected males slightly more than females; children in the first decade of life and adults over 60 more than young adults. The common practice of using many agents in combination makes it exceedingly difficult to learn from experience, for it becomes impossible to determine which agent is associated with a very high death rate. Very large numbers of cases must be collected to prove facts in anæsthesia, for "clinical impressions" are quite unsound. It is estimated that a surgical patient entering hospital has one chance in 75 of dying and that anæsthesia is a primary or important contributing cause in one death in 1,560, a ratio that represents at least 5,128 deaths from anæsthesia in the United States annually, or 3.29 per 100,000 population. The deaths from anæsthesia are twice those from poliomyelitis.

The great changes that occurred in the use of anæsthetic agents and techniques during five years show that the practice of this specialty is far from achieving stability.

BURNS PLEWES

OBSTETRICS AND GYNÆCOLOGY

A B O Blood Groups and Toxæmia of Pregnancy.

PIKE, L. A. AND DICKINS, A. M.: BRIT. M. J., 2: 321, 1954.

The distribution of blood groups in 3,651 admissions to a maternity hospital has been studied. These admissions included 541 patients suffering from toxæmia of pregnancy. As compared with the non-toxæmic patients, the toxæmic patients showed a significant excess of women of group O. Some possible implications are discussed.

Ross MITCHELL

Results of a Planned Attack on Carcinoma of the Vulva.

WAY, S.: BRIT. M. J., 2: 780, 1954.

Owing to the comparative rarity of carcinoma of the vulva, few see sufficient cases to become very familiar with the problems concerned in its treatment. After research into the causes of failure to cure the disease, an experiment was tried in which all the cases in a wide area were referred to one surgeon, who applied a more extensive operation based on the lessons of the preliminary research. The results of the treatment of 79 cases seen before March 31, 1949, are reviewed.

One patient refused treatment and 13 were considered unfit. The operability rate was 83%. The absolute five-year survival rate—that is, the survival of all cases operated on—was 74%. When the lymph nodes were involved the five-year survival rate was 48% and when they were not involved it was 86%.

These figures are a great improvement on other published figures. It is believed that they are well within the reach of any centre which decides to pool its cases so that a special team may carry out a radical approach to the disease.

Ross MITCHELL

PÆDIATRICS

Roentgen Studies in Suppurative Pneumonia of Infants and Children.

CAMPBELL, J. A., GASTINEAU, D. C. AND VELIOS, F.: J. A. M. A., 154: 468, 1954.

The authors point out that though the over-all incidence of this type of pneumonia in infants and young children is only 10%, it does account for a high morbidity and mortality rate. Even with antibiotics the mortality rate is still 33% in children and 40% among infants. Its great morbidity is attributable to the overwhelming toxicity, the tendency to form pulmonary abscesses, pleural complications, and metastatic phenomena. Not only do the invading organisms attack the alveolar walls, peribronchial tissues, and interstitial structures, but also the alveoli themselves. Added to the reduction of the patient's vital capacity is the suffocating effect of bronchial œdema and parenchymal necrosis.

The disease occurs chiefly by bronchogenous invasion and the causative organism is found in the majority of cases to be *Staph. pyogenes* var. *aureus*, although it may also follow as a complication of virus infections and epidemic influenza. Only isolation of the organism in pure culture from the lung or pleural cavity constitutes reliable proof of etiology. However, certain distinctive x-ray features are seen during the development of the pneumonia. These are not present in all cases and do not occur in any regular sequential order. The radiograph is rapidly changing and may often be out of proportion to the clinical course. The sudden appearance of pneumatoceles on a radiograph which previously revealed no area of rarefaction virtually proves the existence of this type of pneumonia when found in a young infant, and it makes the diagnosis probable when encountered in a young child. Surgery is unwarranted since in most experiences these cysts disappear spontaneously. The existence of a nontraumatic pneumothorax in an infant should immediately suggest the presence of a suppurative pneumonia until proven otherwise. The authors point out that although unequivocal diagnosis is never justified on x-ray examination alone, this will help to cut the high infant mortality and supply the physician with an earlier diagnosis and more specific indications for surgical intervention.

ISABEL M. LAUDER

A Current Approach to Strabismus.

REGNIER, E.: POSTGRAD. MED., 15: 463, 1954.

The author states very definitely that cases of strabismus which correct themselves are very few and far between. Thus, the old and comforting standby: "He'll grow out of it," has lost much of its appeal. The widespread belief that the time to treat the squinting child is when he enters school is also wrong. It is not just a mere matter of two eyes being out of line mechanically—it is too often the result of a faulty visual habit pattern.

A primary reason why strabismus has not received more attention is that it usually leaves vision good in one eye, so that the squinting child apparently has normal sight. Strabismus embraces three major liabilities: (1) inferior vision in one of the eyes (the "crossed" one); (2) cosmetic lack of straightness of the eyes, and (3) incapability of achieving the highest levels of visual function that only binocular vision can bring—such as perfect depth perception. The family doctor, although he knows that his professional brothers differ somewhat among themselves as to proper treatment, will be doing a service if he can see that treatment is initiated immediately, since the child will make greater progress in overcoming the handicap in the first years of life. Treatment is limited to: (1) occlusion or eye-patching, (2) the wearing of spectacles, and (3) surgery on the extra-ocular muscles. These are all feasible for an infant of one year, whereas orthoptics can be of little benefit before the age of six since it requires the active co-operation of the child. Techniques must be tried and if proven unsuccessful within three or four months abandoned for a new one. Why let the child go on wearing glasses for ten years if he is not gaining any benefit? Surgery too often reduces mobility of the eye, and disregards the fact that strabismus is often a defect in the co-operative function of the eyes and not in the anatomy of one eye. Supervision of the child with this handicap must continue for months and years, and the parents and doctors must keep in mind that the fault may be a cerebral one.

ISABEL M. LAUDER

THERAPEUTICS

BAL Therapy of Acute Porphyrinuria.

PETERS, H. A.: NEUROLOGY, 4: 477, 1954.

The author describes a case of acute porphyrinuria in a 53 year old woman. She was admitted in a disorientated, hallucinatory state with signs of peripheral neuropathy: ACTH had no effect on her downward progress which included motor paralysis, dysphagia, tremors and alternating hypertension and hypotension. Finally when the patient was *in extremis* BAL was administered, and an hour after the second dose had been given (two and a half hours after the first dose) the patient recovered consciousness and became coherent. BAL was continued in daily doses of 1½ c.c. for ten days, and the abnormal porphyrins disappeared from her urine with improvement of her clinical condition. The patient was eventually discharged on a weekly injection of BAL, and at follow up a month later she was continuing to show improvement.

The author speculates on the etiological factors involved, and suggests that BAL may act by removal of zinc or another heavy metal which may be the primary cause of acute porphyria. He concludes with the observation that BAL administration seemingly reversed the course of this terminal case of acute intermittent porphyria. W. F. T. TATLOW

INDUSTRIAL MEDICINE

Colds Among Office Workers . . . An Epidemiological Study.

REID, D. D., WILLIAMS, R. E. O., HIRCH, A. AND PETTS, M.: LANCET, 2: 1303, 1953.

In this article the authors report a pilot study which they made principally to explore a method of obtaining precise information on the incidence of colds and similar affections among groups of office workers. Their aim was to relate the incidence of colds to certain environmental conditions, including the bacterial content of the air. The workers studied were members of the clerical staff of the General Post Office in several offices in central London. They were questioned weekly during the year April 1949 to March 1950 about their "cold" experience and at the same time observations were made on the bacterial content of the office air, and on the temperature and humidity in the offices. Complete detailed records were obtained of the experience of 131 persons over the whole year.

After explaining the method of systematic interviewing adopted in this study, and also the method of objective measurement of environmental conditions and bacterial contamination of the air, the authors discuss their findings. A series of tables and charts is included. The results indicate that, on the average, each person had 2.2 colds in the year.

Persons with colds remembered contact with someone else who had a cold more often than did "controls" who had had no recent cold. In the authors' opinion this may mean that in some cases the recognized contact was the source of the cold, but it may also be that persons with colds are more likely to recall contacts than are those without colds. The incidence of "colds" appeared to be highest in young women.

There was evidence of short-term immunity following a cold but no other differences in range of contact at work, in travelling, or at home appeared to affect the attack rate. The size of the office populations showed no relation to the risk of having "colds". There was a suggestive time correlation between the onset of the sharp November outbreak of colds and a sudden fall in outside temperature and humidity. During the same week there was a sharp rise in the numbers of mouth streptococci in the air of the offices. MARGARET H. WILTON

FORTHCOMING MEETINGS

CANADA

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS, Winnipeg, Manitoba. (Dr. P. H. T. Thorlakson, Chairman.) April 25-26, 1955.

CANADIAN HOSPITAL ASSOCIATION, Biennial Meeting, Ottawa, Ont. (Executive Director: Dr. W. D. Piercey, 280 Bloor Street West, Toronto 5, Ont.) May 9-11, 1955.

COMMONWEALTH MEDICAL CONFERENCE OF THE BRITISH MEDICAL ASSOCIATION, Toronto, Ontario. (Dr. A. D. Kelly, Canadian Medical Association, 244 St. George Street, Toronto 5.) June 14-16, 1955.

BRITISH MEDICAL ASSOCIATION, CANADIAN MEDICAL ASSOCIATION, ONTARIO MEDICAL ASSOCIATION, Conjoint Meeting, Toronto, Ont. (Dr. A. D. Kelly, General Secretary, Canadian Medical Association, 244 St. George Street, Toronto 5, Ont.) June 17-24, 1955. (Scientific Sessions June 20-24.)

CANADIAN ACADEMY OF ALLERGY, Annual Meeting, Royal York Hotel, Toronto, Ont. (Dr. P. A. Ryan, Acting Secretary, 229 St. Clair Avenue West, Toronto 7, Ont.) June 21, 1955.

UNITED STATES

CONFERENCE ON OCCUPATIONAL CHEST DISEASES, Saranac Lake, New York. (The Secretary, Saranac Laboratory, New York, N.Y.) February 7-9, 1955.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS, Hotels Cleveland and Hollenden, Cleveland, Ohio. (Dr. Stanley O. Hoerr, Chairman.) February 21-24, 1955.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION, Annual Meeting, Hotel Sherman, Chicago, Ill. (Marion F. Langer, Ph.D., Executive Secretary, 1790 Broadway, New York 19, N.Y.) February 28 to March 2, 1955.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS, Sheraton-Biltmore Hotel, Providence, Rhode Island. (Dr. Henri E. Gauthier, Chairman.) March 3-5, 1955.

EIGHTH ANNUAL POSTGRADUATE COURSE ON DISEASES OF THE CHEST, Bellevue-Stratford Hotel, Philadelphia, Pa. (Dr. C. L. Jackson, Chairman.) March 7-11, 1955.

INTERNATIONAL SYMPOSIUM ON CARDIOVASCULAR SURGERY, Henry Ford Hospital, Detroit, Michigan. (Dr. Conrad R. Lam, Chairman of Programme Committee, 2799 West Grand Boulevard, Detroit 2, Michigan.) March 17-19, 1955.

AERO MEDICAL ASSOCIATION, Twenty-sixth Annual Meeting, Hotel Statler, Washington, D.C. (Dr. O. O. Benson, Jr., Brigadier General, U.S.A., President.) March 21-23, 1955.

AMERICAN ACADEMY OF GENERAL PRACTICE—7th Annual Scientific Assembly, Los Angeles. (Mr. Mac F. Cahal, Broadway at Thirty-fourth, Kansas City 11, Missouri.) March 28-31, 1955.

AMERICAN DERMATOLOGICAL ASSOCIATION, Belleair, Florida. April 17-21, 1955.

AMERICAN RADIUM SOCIETY, Annual Meeting, Shoreham Hotel, Washington, D.C. (Dr. R. E. Tricke, Secretary, Mayo Clinic, Rochester, Minn.) April 21-23, 1955.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Shoreham Hotel, Washington, D.C. (Dr. E. P. Pendergrass, Secretary-General, 3400 Spruce Street, Philadelphia 4, Pa.) April 24-29, 1955.

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AMERICAN COLLEGE OF PHYSICIANS, Philadelphia, Pa. (Mr. E. R. Loveland, Executive Secretary, 4200 Pine Street, Philadelphia 4, Pa.) April 25-29, 1955.

AMERICAN PSYCHOSOMATIC SOCIETY, Annual Meeting, Atlantic City, N.J. May 4-5, 1955.

AMERICAN UROLOGICAL ASSOCIATION, Biltmore Hotel Los Angeles, California. (Dr. C. H. de T. Shivers, Secretary, 121 S. Illinois Ave., Atlantic City, N.J.) May 16-19, 1955.

OTHER COUNTRIES

PAN-AMERICAN ACADEMY OF GENERAL PRACTICE, Lima, Peru. (Dr. Arturo Martinez, Secretary, 54 East 72nd Street, New York 21, N.Y.) February 11-25, 1955.

LATIN AMERICAN CONGRESS OF PHYSICAL MEDICINE, Lima, Peru. (Dr. Cassius de Victoria, Executive Director, 176 East 71st Street, New York, N.Y.) February 14-19, 1955.

SIXTH LATIN AMERICAN NEURO-SURGICAL CONGRESS AND SECOND LATIN AMERICAN ELECTROENCEPHALOGRAPHICAL CONGRESS, Montevideo, Uruguay. (Dr. R. Arana-Iniguez, Convencion 1287, Montevideo, and Dr. P. Pinto Pupo, San Pablo, Brazil.) March 21-24, 1955.

JAPAN MEDICAL CONGRESS, Kyoto, Japan. (Dr. M. Goto, Secretary General, University Hospital, Medical Faculty of Kyoto University, Kyoto, Japan.) April 1-5, 1955.

TENTH CONGRESS OF THE INTERNATIONAL UROLOGICAL SOCIETY, Athens. (Prof. Z. Kairis, rue Voukourestiou 25, Athens.) April 10-18, 1955.

MIDDLE EAST MEDICAL ASSEMBLY OF THE AMERICAN UNIVERSITY OF BEIRUT, American University campus, Beirut, Lebanon. (Dr. John L. Wilson, Professor of Surgery, Chairman, Committee for the Fifth Middle East Medical Assembly.) April 22-24, 1955.

WORLD HEALTH ORGANIZATION—8th General Assembly, Mexico City. (World Health Organization, Palais des Nations, Geneva, Switzerland.) May 10, 1955.

FIFTEENTH CONGRESS OF FRENCH-SPEAKING PÆDIATRICIANS, Marseilles, France. (Dr. Réné Bernard, Clinique Médicale Infantile, Hôpital de la Conception, Marseilles.) May 23-25, 1955.

INTERNATIONAL COLLEGE OF SURGEONS—20th Anniversary Meeting, Geneva, Switzerland. (Dr. Max Thorek, 850 West Irving Park Road, Chicago 13, Ill.) May 23-26, 1955.

SEVENTH INTERNATIONAL CONGRESS OF COMPARATIVE PATHOLOGY, Lausanne, Switzerland. (Prof. Hauduroy, 19 avenue César-Roux, Lausanne.) May 26-31, 1955.

INTERNATIONAL HOSPITAL CONGRESS, Lucerne, Switzerland. (Capt. J. E. Stone, Hon. Secretary, International Hospital Federation, 10 Old Jewry, London, E.C.2, England.) May 30-June 3, 1955.

EUROPEAN CONGRESS ON RHEUMATISM, Scheveningen, The Hague, Netherlands. (Dr. H. van Swaay, Secretary, Pieter Bothstraat 12, The Hague, Netherlands.) June 13-17, 1955.

FIFTH CONGRESS OF THE INTERNATIONAL ASSOCIATION FOR THE STUDY OF THE BRONCHI, Stockholm, Sweden. (Dr. J. M. Lemoine, 187 boulevard Saint-Germain, Paris 7e.) June 18-19, 1955.

FOURTH COMMONWEALTH HEALTH AND TUBERCULOSIS CONFERENCE, Royal Festival Hall, London, England. (Secretary-General, National Association for the Prevention of Tuberculosis, Tavistock House North, Tavistock Square, London, W.C.1, England.) June 21-25, 1955.

NEWS ITEMS

BRITISH COLUMBIA

Dr. G. F. Amyot, deputy minister of health, has announced that 40,000 five- and six-year-old B.C. children will be given the Salk anti-poliomyelitis vaccine during March. Of these a half will be from the Lower Mainland. While the incidence of poliomyelitis during 1954 has been on the whole low, the object of this vaccination, Dr. Amyot states, is to anticipate the dangers of warmer weather by giving the vaccine early in the year. The cost will be shared by the Provincial and Federal Governments, with the B.C. Polio Foundation contributing to the cost of the vaccine. The giving of the vaccine will, of course, be subject to the consent of the parents.

Dr. George Elliot, assistant provincial medical health officer, feels that the evidence to date is sufficient to warrant wide use of the vaccine.

Hospital bed shortage is again a matter for press comment. All hospitals on the Lower Mainland are operating at capacity or over, and many regularly have extra beds.

The new Burnaby Hospital is building an addition of 120 beds or so, but expects this to be quite inadequate for the needs of the growing municipality.

North Vancouver is talking of a new hospital to supplement the old one, which is heavily overtaxed: and there is at present no relief in sight for the Vancouver area.

The recent March of Dimes campaign in Vancouver realized over $100,000 towards the support of the Children's Hospital, thus exceeding the quota which had been set.

J. H. MACDERMOT

MANITOBA

Dr. John Hildes has resigned as medical director of Winnipeg's municipal hospitals. On January 1 he became director of an Arctic medical research unit, set up by the Defence Research Board, in the department of physiology and medical research at the medical school of the University of Manitoba. His work will include research into the medical aspects of living in Arctic regions. For his work during the poliomyelitis epidemic of 1953, Dr. Hildes was chosen "Man of the Year" by the readers of the *Winnipeg Tribune*.

Dr. John Alcock will be acting medical director of the municipal hospitals until a new appointment is made.

Dr. John Silinsky, a graduate of Shanghai University, China, and Dr. Henry Walters, a graduate of Frankfurt University, Germany, who recently passed the Dominion Council examinations, have been appointed to the medical staff of Clearwater Lake Sanatorium.

The advantages of having routine chest x-ray films of patients admitted to general hospitals in this province are now being realized. Fifty-nine general hospitals have entered into agreements with the Sanatorium Board of Manitoba to take free routine chest films of patients admitted to the hospital. The Board reimburses the hospital for the cost of this service out of an appropriation from the National Health Grant.

Probable tuberculosis, apparently active, was diagnosed in 68 in-patients and in 8 out-patients. All these patients were given necessary advice and treatment.

One person in every 766 examined probably had tuberculosis, apparently active. In community x-ray surveys of apparently healthy people, only one in 5,500 had active tuberculosis. In 3,965 chest x-ray examinations given to members of general hospital staffs not a single case of active tuberculosis was discovered. This

is a marked contrast to the findings of a few years ago before the present programme was functioning.

Sir James Learmonth, professor of surgery in the University of Edinburgh, and Sims professor of surgery for the British Commonwealth, spent a busy week in Winnipeg toward the end of November. He gave several lectures to medical students and addressed staff conferences at the University, also at St. Boniface, Children's, Winnipeg General and Deer Lodge hospitals. On November 26 he spoke to the Winnipeg Medical Society and was presented with a silver tray bearing the coat of arms of the University of Manitoba.

Ground has been broken for the new library of the Medical College. Plans call for an auditorium in the building in which the Winnipeg Medical Society and kindred societies may meet. The Winnipeg Medical Society has given a grant to aid in the furnishing of the auditorium.

On December 1 a farewell dinner was given at Manitoba Club to three members of the honorary attending surgical staff of the Winnipeg General Hospital who have retired from active duty. They are Dr. C. W. Burns, past president of the Canadian Medical Association; Dr. M. R. MacCharles, surgeon to the hospital; and Dr. H. D. Morse, chief of the Department of Urology. Each was appointed to the honorary consulting staff. Dr. P. H. T. Thorlakson presided, and Mr. W. A. Murphy, president of the Board of Directors, Mr. A. E. Johnston, secretary-treasurer, and Dr. L. G. Bell, dean of the Faculty of Medicine, spoke in appreciation of the work of the surgical staff. Dr. Burns and Dr. MacCharles responded. Through illness Dr. Morse was unable to be present.

ROSS MITCHELL

ONTARIO

Dr. R. M. Mitchell presided at the official opening of the new home of the Ontario Medical Association at 244 St. George Street, Toronto, on December 6. The dedication prayer was offered by his father, the Rev. R. A. Mitchell, who was that day celebrating his eighty-sixth birthday.

Dr. M. C. Harvey, chairman of the Association Home Committee, told of the long search for a suitable, centrally located building. He described the work of remodelling and redecorating the old-fashioned but spacious house, transforming it into comfortable offices now shared with the Canadian Medical Association.

The Honourable Mackinnon Phillips, M.D., Minister of Health, unveiled a plaque in recognition of the contribution by the officers, directors and members of the O.M.A. past and present, whose foresight, wisdom and untiring efforts made possible the permanent home.

Dr. T. C. Routley recalled that the O.M.A. was organized in 1880. When he became secretary in 1918 the treasury held eight dollars. The first office was situated in the attic of his home. In 1921 the establishment had the first paid office assistant, Mrs. Mabel J. Campbell (present at the opening ceremony), who was with the O.M.A. and later with the C.M.A. until her recent retirement. The O.M.A. now has an office staff of seven in addition to the secretary. The membership numbers 4,355.

In 1924 the University of Toronto gave the O.M.A. office space rent-free at 184 College Street. This happy circumstance continued until 1946, when the next move was to the Blue Cross building on St. Clair Avenue West; in September 1953, the present building at 244 St. George Street was ready for use.

After Dr. Routley spoke, the Lieutenant-Governor, Louis O. Breithaupt cut the ribbon and declared the building open. Excellent refreshments were served by the Women's Auxiliary, whose president is Mrs. M. C. Harvey.

On December 8 in the village of Ayr, Waterloo County, a goodly number of citizens, friends, patients and colleagues gathered to honour Dr. Ward Woolner, who has faithfully served the community as a physician for half a century. Councillor John Dance, who was the first baby he delivered, presented Dr. Woolner with an illuminated scroll on behalf of the residents. Mrs. Woolner was there to share the honours with her husband. They had five children. One is Dr. James Woolner of Hamilton; another son was killed overseas with the R.C.A.F.

Dr. Woolner went to the community in 1904. In addition to his duties as family physician to a large section of that historic rural community he found time to serve on the School Board, on the Town and County Council, as health officer and as a member of the Board and Session of his church.

In wider fields he became District Deputy Grand Master of the Masonic Order, president of the Ontario Medical Association, president of the Ontario Health Officers Association, and, lastly, president of the Ontario College of Physicians and Surgeons. All this represents a great volume of service outside the ordinary path of duty.

Among those who gathered to pay their tribute were Dr. T. C. Routley, Canadian Medical Association; Dr. James Dauphinee, College of Physicians and Surgeons; Dr. Glenn Sawyer, Ontario Medical Association; Dr. James Fisher, Kitchener Academy of Medicine; Dr. M. C. Harvey, Kitchener; Dr. E. J. Clifford, Toronto, and many other physicians.

The Oakville-Trafalgar Memorial Hospital has been chosen by civil defence and Canadian hospital officials as a model for small institutions in disaster planning. With local police and civil defence officials, such matters as alternate routes for reaching the hospital have been worked out. Inside the hospital the emergency adjustments that a disaster would entail have been studied in detail.

Hamilton General Hospital has been selected as the model large hospital in disaster planning.

The new Jewish Home for the Aged, built at a cost of $2,500,000, has been opened on the northern edge of Toronto. The new building incorporates Baycrest Hospital, which is to be a major centre for geriatrics. It is affiliated with Mount Sinai Hospital. There is accommodation for 165 people in the home and for 87 in the hospital. The 25 acres of surrounding grounds provide a pleasant vista. In every sitting room there is a television set. There are solariums, a tuck shop, a library and occupational therapy rooms with trained therapists to teach crafts and hobbies.

Dr. B. H. McNeel has been appointed director of community health services for Ontario. Dr. McNeel was formerly superintendent of the Ontario Hospital, St. Thomas.

Dr. C. A. Cleland, superintendent of Ontario Hospital, Toronto, will take over at St. Thomas.

Dr. D. O. Lynch, Kingston, has been named superintendent of the hospital in Toronto.

Dr. C. H. McCuaig, professor of psychiatry, Queen's University, has been appointed superintendent at Kingston.

The Canadian Foundation for Poliomyelitis in its annual March of Dimes campaign in Ontario will set an objective of $350,000. The money will be used for research, rehabilitation of poliomyelitis victims and provision of special equipment needed by paralyzed patients.

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The case rate in Ontario seems to be high and low on alternate years. In 1949 there were 1,138 patients. In 1950, this figure dropped to 376. Cases rose to 1,701 in 1951 and dropped in 1952 to 705. In 1953 there was a rise to 2,239 cases and in 1954 a drop to only 300.

Dr. Brian A. Cookson, department of surgery, addressed the Physiological Society, University of Toronto, on "Cardiac Failure in Severe Hypothermia and its Relief by Quaternary Compounds."

Dr. H. J. Barrie, department of pathology, addressed the Toronto Diabetes Association on "The Kimmelstiel-Wilson Syndrome and Some Interrelations in Renal Disease."

Dr. H. M. Bain, Hospital for Sick Children, described his clinical experience with "lente-type" insulin. During the past year 25 children with unstable diabetes have been given this type of insulin. It results in smoother control; when a reaction occurs, it is mild and has warning signs. There is less local allergy. The disadvantage is the morning hyperglycæmia.

LILLIAN A. CHASE

QUEBEC

The appointment of Jean-Louis Rochefort, M.D., of Trois Rivières and Montreal, as medical director of Blue Cross (Quebec Hospital Service Association) has been announced by E. Duncan Millican, president. Dr. Rochefort graduated in medicine from Laval University, Quebec, after which he continued his studies in New York City with a postgraduate course. He is a member of the executive committee of the Canadian Medical Association, Quebec Division.

SASKATCHEWAN

Dr. A. C. Kanaar has been appointed to a new position as director of physical medicine in the Division of Physical Restoration of the Saskatchewan Department of Public Health. In this post, Dr. Kanaar will be responsible for supervising medical treatment at the Physical Restoration Centre in Regina and Saskatoon.

It was reported in November that more than 10,000 hospitalization cards for 1955 have yet to be taken out in Saskatoon. The city tax collector reported that 19,909 cards had been issued to November 30, this year's deadline for the first instalment on hospitalization payments.

Physicians who are interested in hunting might note with pleasure that, according to a statement of Game Commissioner E. L. Paynter, the mallard duck population is apparently too numerous in this area, and also that the Hungarian partridge is not "harvested enough in Saskatchewan."

Mr. Paynter also reported that 34 hunters have been shot this season in Saskatchewan, 13 dying from their injuries.

The first group of 17 nurses from Britain arrived recently in Saskatoon and were received by hospital officials. Good reports of their nursing ability have been received from the hospitals conducting the period of orientation.

The Western Canada Institute for Hospital Administrators will be held in Alberta, June 13 to 18, 1955.

G. W. PEACOCK

BOOK REVIEWS

THE THYROID

T. Levitt, Hunterian Professor of the Royal College of Surgeons of England; Lecturer in Surgery to the Fellowship of Postgraduate Medicine at the New End Hospital, Hampstead, London. 606 pp. illust. $17.90. E. & S. Livingstone Ltd., Edinburgh and London; The Macmillan Company of Canada Ltd., Toronto 2, 1954.

In his preface the author quotes from his own Hunterian Lecture of 1952: "Nothing is static. Change is constant, not only in the sequence of life but also in the understanding thereof. To accept meekly and to repeat slavishly the time-honoured clinical beliefs of the past, without reassessment, spells retrogression. This is nowhere more apparent than in the field of Endocrinology in general and thyroid disease in particular."

On this premise and on the sound basis of 24 years of experience, and the detailed and critical investigation of 2,000 thyroidectomies, the writer has built this work. In it he offers his concept of the whole natural history of thyroid disease "in its sequence from life to death." The clinical manifestations are examined in relation to the natural history. The various methods of diagnosis and treatment, including the use of radioactive iodine, are critically assessed. Operative techniques are described in detail and illustrated profusely. Throughout it is the difficult and perplexing problems of thyroid disease which are stressed.

In an attempt to correlate better the clinical findings with the macroscopic and microscopic appearance of the diseased gland, the author establishes a new nomenclature and uses it throughout.

The book is magnificently illustrated with diagrams, photomicrographs, and photographs in monochrome and colour.

It seems inevitable that for the present, in any case, and probably for some years to come this volume will be accepted as the definitive treatise on the thyroid, its function and dysfunction.

LECTURES ON THE THYROID

J. H. Means, Jackson Professor of Clinical Medicine Emeritus, Harvard University; Former Chief of Medical Services, Massachusetts General Hospital; Physician, Massachusetts Institute of Technology. 112 pp. illust. $3.30. Harvard University Press, Cambridge; S. J. Reginald Saunders & Co. Ltd., Toronto, 1954.

This book contains five lectures on various aspects of the thyroid gland by the world-famous Boston authority. The lectures do not constitute a course on thyroid disease but are designed to round out the knowledge of those already acquainted with the subject, and to start them thinking by drawing attention to unsolved problems, and making suggestions for future research. Dr. Means first discusses the integrative action of the endocrine system with particular reference to the pituitary-thyroid and pituitary-adrenal axes. Speaking of the interplay of endocrine organs, he says:

"In a system made of infinitely interrelated mechanisms, as in the animal body, or at least the bodies of higher animals, one cannot alter any one part of the mechanism without altering the rest, for the rest must adjust to the disturbed part in order that commotion in the whole be kept at a minimum. Those physicians and surgeons who deal with a very restricted part of the body would do well from time to time to ponder these truths."

In a lecture on the thyroid hormone, Dr. Means suggests lines for research, including study of the iodine-

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trapping mechanism, development of an easy method of determining thyrotropin titre in the blood, and study of the evolution of thyroxine in the animal kingdom. He discusses the use of hormones, drugs and radiation in therapy, casting doubt on the value of thyroid extract in malignant exophthalmos but supporting its use in sterility and habitual abortion. He states frankly that he is worried about the possibility of producing cancer with radio-iodine: "Only until more years elapse and more patients are treated shall we feel that this ghost has been laid permanently."

In a very interesting discussion on the etiology of Graves's disease, he speculates on the relationship of ophthalmopathy to the thyroid, taking the position that the eye signs in this disease are not signs of thyrotoxicosis but that ophthalmopathy and thyrotoxicosis are both manifestations of Graves's disease.

The last chapter deals with the need for iodine; in Dr. Means's view, a sixty-four dollar question in thyroidology is the nature of the peculiar action of iodine in Graves's disease. Whereas administration of iodine to a person with endemic goitre may cause thyrotoxicosis, administration in Graves's disease has the reverse effect. This and the many other questions raised by Dr. Means should keep investigators busy for a long time ahead. On the other hand, anyone who starts to study the thyroid without reading this book is missing something of value.

TUBERCULOSIS IN CHILDHOOD AND ADOLESCENCE

F. J. Bentley, Senior Physician; S. Grzybowski, Senior Registrar, High Wood Hospital for Children, Brentwood, Essex; and B. Benjamin, formerly Statistician, London County Council. 259 pp. illust. $5.00. National Association for the Prevention of Tuberculosis, London, 1954.

This book presents an analysis of 1,049 consecutive cases of tuberculosis in children treated at the High Wood Hospital, England. during the years 1942-1946, who were discharged or died there. The survivors were followed up during 1949-1952. All manifestations of tuberculosis in children are represented, but special reference is made to the pulmonary forms of the disease. The book is divided into twenty-two chapters dealing with such topics as simple primary pulmonary tuberculosis, segmental lesions, pleural effusion, and miliary tuberculosis. The subdivision of simple primary tuberculosis into mediastinal lymph node enlargement with and without radiological visibility of the primary focus is convenient for the purpose of analysis. The authors emphasize that very large nodes in certain areas of the chest, for instance, at the bifurcation of the trachea, may remain unseen and children with very large mediastinal nodes are apt to produce segmental lesions but the prognosis is no worse than that of the remainder.

The incidence, pathogenesis, pathology, clinical course, radiological appearance and progress of the lobar or segmental lesions are discussed briefly. The figures suggest that approximately 5 to 10% of children with primary pulmonary tuberculosis will develop a segmental lesion. The authors stress that much more work, including repeated bronchography, has to be done before any definite conclusions on the subject of bronchiectasis following primary pulmonary tuberculosis can be reached. Special stress is laid on the difficulties and importance of the diagnosis of miliary tuberculosis. Tuberculous meningitis and miliary tuberculosis accounted for 92% of the total deaths in their series. Since the advent of potent antituberculous drugs the outlook in these two conditions has greatly improved.

A few words are devoted to skeletal tuberculosis, cervical adenitis, tuberculous peritonitis, renal tuberculosis, tuberculosis of the skin and phlyctenular conjunctivitis. Erythema nodosum and its relation to primary infection are briefly touched on. The alleged adverse effect of measles and whooping cough on the course of primary pulmonary tuberculosis is considered. The possible connections between primary tuberculous infection in children and pulmonary tuberculosis in adults are also considered. The management of minimal pulmonary lesions is well covered.

All chapters are followed by a brief summary of the authors' conclusions. References are numerous. The text and format of the book and the paper are good; the printing is clear and easy to read. The diagrams illustrate clearly what they are meant to clarify and the quality of the radiological reproductions is good. This book contains much of interest and value to all physicians who are concerned with tuberculosis in childhood.

SIGMUND FREUD: LIFE AND WORK. VOL. I

The Young Freud 1856-1900. E. Jones. 454 pp. illust. The Hogarth Press, London, 1953.

The nature of Sigmund Freud's contributions to science is such as to attract the ill-informed muck-raker, who, as is usual in this world, tends to be believed. It is a matter for rejoicing, therefore, that one of Freud's intimate friends, Dr. Ernest Jones, the doyen of British psychoanalysis, has taken upon himself the difficult task of preparing a definitive biography intended to clear away the many misconceptions current about the great psychoanalyst. The first volume—now published—takes the story up to 1900 when Freud at the age of 44 was emerging from a self-analysis, shedding his neurotic doubts and fears, and starting on the serene and confident course of his later life. Dr. Jones warns us that this is not intended to be a popular biography of Freud, and indeed it would make difficult reading for those not acquainted with psychiatry. The account is, however, extremely well written and should not be neglected by any serious student of Freud's work.

Freud's contributions to neurology are set forth in detail (it is not generally known that he was a world authority on cerebral palsy), and the biographer shows how Freud gradually made the break with neurophysiology. The facts about the cocaine episode, in which Freud just missed being hailed as the discoverer of local anæsthesia, are set out in full.

Dr. Jones traces the changing relationships of Freud to Breuer, who gave him great material help and encouragement, and to Fliess, for whom Freud had a passionate attachment over a number of years. In these chapters the biographer brings out well Freud's need for periodic experiences of intense love and hate.

The first volume closes with an account of Freud's theory of the mind, in which Dr. Jones suggests that a comparison of Freud's sketch of cerebral physiology written in 1894 with recent electronic theories of cerebral functioning would be of interest.

PORPHYRINS

Their Biological and Chemical Importance. A. Vannotti, University Professor and Director of the University Medical Polyclinic, Lausanne. 258 pp. illust. 50/-. Hilger & Watts, Ltd., Hilger Division, London, N.W.1, 1954.

Europeans have, in the main, preceded us by many years in their interest in the biological significance of porphyrins. This book is particularly valuable, because it extracts for us the voluminous European literature on this subject. Various short chapters on the more academic phases of porphyrin chemistry and physiology finally lead to a longer and very informative chapter on the porphyrin diseases. The author leaves no doubt that the porphyrins actually cause the symptoms of the disease and are not merely parallel phenomena. Professor Vannotti's book will be attractive to all those who are interested in porphyrins, either in the laboratory or in the clinic.

Pigmented mole, preoperative.

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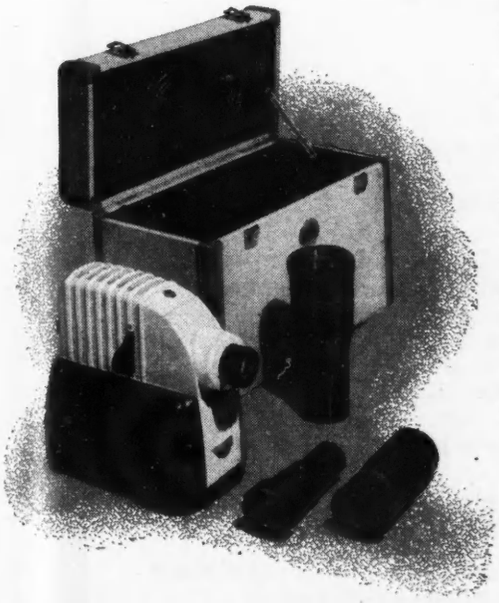

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CLINICAL MEDICINE IN GENERAL PRACTICE

Edited by J. Fry. 436 pp. $4.70. J. & A. Churchill Ltd., London; British Book Service (Canada) Ltd., Toronto 6, 1954.

Dr. Fry, a family physician in Kent, England, with the help of a number of other general practitioners has attempted to bring together information of value to the medical student and house officer intending to enter general practice.

The book is based on conditions in England today, and it contains useful hints for those who enter practice in that country. It is of limited value on this side of the Atlantic. It makes interesting reading, in a general way, about topics with which the family physician is concerned. The accumulated experience of the contributors brings out many points worth adding to our knowledge. The treatment of the various subjects is necessarily restricted in a book of this small format.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

Specially commissioned articles from the British Medical Journal. 2nd Collection. 570 pp. illust. 25/-. British Medical Association, London, W.C. 1, 1954.

This second volume of short essays, previously published in the *British Medical Journal* and intended to bring general practitioners up to date on certain subjects, is of interest as regards the distribution of the material. It reflects to a certain extent—perhaps involuntarily, but more likely purposely—deficiencies in the training of medical students. Thus no less than nine articles are on subjects related to the locomotor system and usually poorly understood by recent graduates, such as backache, the painful shoulder, spinal deformities in children, and the principles of physical medicine. There are, in contrast, only four articles on other aspects of surgery. Dermatology, psychiatry and the eye, ear, nose and throat group of specialties also receive a considerable share of attention. The most unusual contribution (and by a surgeon, too) is on the basic principles of atomic structure. This little book will help to fill a number of gaps in the average medical man's knowledge. It has, of course, received the usual careful preparation given to B.M.A. publications.

MEDICAL USES OF CORTISONE

Including Hydrocortisone and Corticotropin. Edited by F. D. W. Lukens, Professor of Medicine, University of Pennsylvania School of Medicine; Director, The George S. Cox Medical Research Institute, University of Pennsylvania, Philadelphia, Pennsylvania. 534 pp. illust. The Blakiston Company, Inc., Toronto; Merck & Co. Ltd., Montreal, 1954.

This survey consists of 15 chapters by 29 authors covering the physiology, pharmacology and clinical applications of the adrenal cortical and corticotropic hormones in man. The opening chapter gives a detailed account of the chemistry of these hormones and their biochemical effects. Thorn and his associates then deal with the pharmacology, particularly in cortical insufficiency. The rest of the chapters have to do with their chemical uses in arthritis, rheumatic fever, collagen diseases, allergy, diseases of the skin, granulomata, infections, diseases of the eye, intestinal tract, blood, kidney and finally in neuropsychiatric disorders. They represent the consensus of authorities in their various fields and as such can be recommended to all practitioners.

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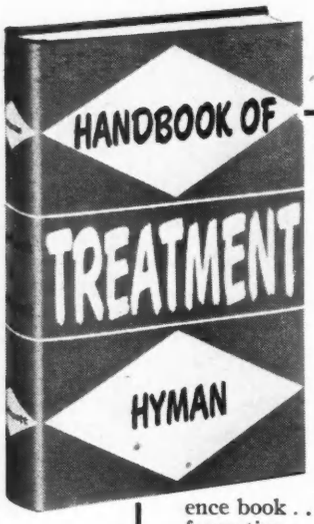

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TEXTBOOK OF THE NERVOUS SYSTEM

H. C. Elliott, Associate Professor of Anatomy, College of Medicine, University of Nebraska. 437 pp. illust. 2nd ed. $9.00. J. B. Lippincott Company, Montreal, 1954.

The second edition of this masterly account of human neuroanatomy and neurophysiology will no doubt receive as enthusiastic a welcome as did the first in 1947. Dr. Elliott has now incorporated many suggestions for the improvement of the book, and has greatly enlarged the atlas. For those who have not encountered the work before, we should explain that this is a text for the student of neurology at any stage. The first part of the book consists of an admirably lucid account of the general structure and function of the nervous system. One can but wish that this had been available to an older generation of students struggling with the complexities of this difficult but fascinating system. Having led the student by developmental paths to a general knowledge of the nervous system, Dr. Elliott then fills in the details in the second part of the book with a wealth of simple diagrams. Finally there are about a hundred pages of photographs and photomicrographs with labelled explanatory diagrams alongside. For the rare inquisitive student, a bibliography is appended to help his further studies.

Anyone who does not understand the nervous system after working through this most enjoyable text must be classed as unteachable.

ATLAS OF CONGENITAL CARDIAC DISEASE

M. E. Abbott, Curator of the Historical Medical Museum and Assistant Professor of Medical Research, McGill University, Montreal, Canada. 62 pp. illust. American Heart Association, Inc., New York, N.Y., 1954.

Dr. Maude Abbott's well-known Atlas of Congenital Heart Disease has been reprinted and is available again. It is still a very useful book in that it contains an analysis of 1,000 postmortem studies of congenital heart disease. She would have enjoyed the rapid growth of diagnosis and surgery in congenital heart disease of the last ten years since her death.

THE PINEAL GLAND. A REVIEW OF THE PHYSIOLOGIC LITERATURE

J. I. Kitay and M. D. Altschule. 280 pp. illust. $5.50. Published for the Commonwealth Fund by Harvard University Press, Cambridge, Mass.; S. J. Reginald Saunders & Company Limited, Toronto, 1954.

This book contains the most comprehensive bibliography of papers on the pineal gland ever assembled. The authors have assessed these papers and organized the report so that they are readily available. The frequent recurrence of such phrases as "incompleteness of the data" and "not conclusively demonstrated" is a sad commentary on medical research methods. This is underlined by the concluding remark of the experimental section: "When extensive, well-controlled, and thorough observations are made, they will undoubtedly contribute to the understanding of pineal function."

Over 160 pages are devoted to the listing of the authors and titles of almost 1,800 papers and reviews. Kitay and Altschule have assembled and sorted a mass of contradictory and incomplete reports. Their final conclusion is: "Although the available physiologic and clinical data justify the presumption that the gland is functional, its functions cannot yet be defined."

It is disappointing that the available data on the pineal as a photic receptor have been omitted, for this is the only obvious gap.